OPTIMISING WARFARIN MANAGEMENT:

AN EXPLORATION OF PHARMACIST-DELIVERED MODELS OF CARE

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DECLARATION OF ORIGINALITY

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ABSTRACT

Warfarin has been the mainstay of preventing and treating thromboembolism for over 50 years and is currently taken by over 200,000 Australians. Optimal management of warfarin relies on regular monitoring of the International Normalised Ratio (INR), appropriate dose adjustment, effective communication and comprehensive patient education. Therapy may be managed by a range of healthcare providers in a variety of settings, and by patients themselves, although management in Australia has tended to focus on traditional office and pathology-based models. Internationally, however, alternative models of care are playing an increasingly significant role with positive results and pharmacists have been shown to be effective in improving the quality use of warfarin through a variety of these service delivery models.

The main objective of this thesis was to examine the effect of using pharmacist-delivered models of care on warfarin management within Australia through a number of complementary projects.

Guidelines recommend aiming for a target INR control of upwards of 70% time in range. Internationally, community-based studies consistently demonstrate suboptimal levels of INR control, although little data is available on the level of control achieved through usual models of care in Australia. A retrospective cross-sectional study of INR results from 442 Australian veterans was undertaken to determine the INR control of a usual care population. The mean time in INR range was 61.8% in this population. This suggests a potential role for strategies aiming to improve INR control among Australian patients in line with best practice guidelines.

Review of the literature suggested pharmacists could play a role in improving warfarin management through optimising the delivery of education, improving access to INR testing and facilitating patient self-monitoring. A series of sub-projects

were designed to develop and pilot tools to support pharmacists in addressing these strategies.

A website was designed to provide patients and health professionals with educational resources regarding anticoagulation. The site aimed to be a comprehensive and reliable online resource and was promoted directly to pharmacists. It received high levels of utilisation, with almost 250,000 views in 12 months, and positive feedback from health professionals and patients, and proved to be an important educational resource that was an easy and accessible tool for pharmacists to use to complement face to face counselling services and further improve patients' knowledge about warfarin therapy.

Tools and resources were developed to improve access to INR testing by facilitating the introduction of anticoagulation services, including pharmacist-delivered INR clinics, in Australia. A pilot was conducted in three rural community pharmacies, with a subsequent project involving 36 pharmacies. While the resources received positive feedback from participating pharmacists, the rate of successful service implementation was low. Despite the perceived benefits to the communities, the current model of healthcare remuneration in Australia impacted on the long term financial viability of such services.

Development, implementation and evaluation of a pharmacy-centred pathway to enable patient self-monitoring (PSM) was also undertaken. Forty-eight patients successfully underwent training and participated in PSM for a median of 16.9 months. INR control data during PSM was compared to that from the six months prior to entering the study for 46 of the 48 patients. There was a significant improvement in INR control, with the mean time in range increasing from 64.0% to 72.9% ($p<0.05$). Clinical data analysis was complemented by a qualitative exploration of 38 patients' experiences of self-monitoring and the impact of PSM on

various aspects of their lives. It was found that patients discussed PSM positively, describing it passionately and as something of value, which reduced their anxiety and freed them to carry on with their lives.

The results of these projects suggest that expansion of the professional services offered by pharmacists has the potential to improve the control of warfarin therapy in Australia. Changes in remuneration for healthcare services are likely to increase the viability of pharmacist-delivered INR services and the uptake of PSM. Despite the arrival of newer oral anticoagulant agents, the use of warfarin is likely to continue for many years. Optimising warfarin management is arguably the safest and most clinically and cost-effective option for preventing and treating thromboembolism at this point in time. Pharmacists can play an important role in improving warfarin management by embracing opportunities to deliver professional services aimed at optimising outcomes for Australians taking warfarin.

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If I have seen further it is only by standing on the shoulders of giants.

Isaac Newton, 1676

While I am certainly under no illusion that the contents of this thesis comes even close to resembling the brilliant work of Newton, the sentiments he expressed in his letter to Robert Hooke strongly echo my own. This thesis, and the work contained within it, would have been unimaginable without the dedicated support and encouragement of a huge number of extraordinary people.

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a Flexible Anticoagulation Monitoring Service for Community Pharmacies project, and to their representatives for arranging onsite training for pharmacies participating in both the Development and Implementation of a Flexible Anticoagulation Monitoring Service for Rural Community Pharmacies project and the follow-up Development and Implementation of a Flexible Anticoagulation Monitoring Service for Community Pharmacies project, and to the Australian Government Department of Veteran's Affairs for providing funding and data for The Current State of Management of Australian Veterans Taking Warfarin project.

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PUBLICATIONS

All publications listed resulted from work described in this thesis

Note: The candidate changed her surname from Jeffrey to van Tienen in early 2010.

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ABBREVIATIONS

AACP	Australian Association of Consultant Pharmacy
ACTRN	Australian Clinical Trials Registry Number
ADR	Adverse Drug Reaction
AF	Atrial Fibrillation
AMA	Australian Medical Association
AMI	Acute Myocardial Infarction
ARISTOTLE	Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation
ATC	Anatomical Therapeutic Chemical
BSL	Blood Sugar Level
$CHADS_2$	Stroke risk calculation tool
CI	Confidence Interval
CPA	Community Pharmacy Agreement
DVA	Department of Veterans Affairs
EQ-5D	A standardised instrument to measure of health outcome
EQC	External Quality Control
GP	General Practitioner
HMR	Home Medicines Review
HR	Hazard Ratio
ID	Identification
INR	International Normalised Ratio
IQC	Internal Quality Control
ISI	International Sensitivity Index
MI	Myocardial Infarction
NEQAS	National External Quality Assessment Scheme
NSW	New South Wales
NZ	New Zealand
PAD	Peripheral Arterial Disease
PBS	Pharmaceutical Benefits Scheme
PGA	Pharmacy Guild of Australia
POC	Point of Care
PoCT	Point of Care Trial
PSA	Pharmaceutical Society of Australia
PSM	Patient Self-Monitoring

PT	Prothrombin Time
QA	Quality Assurance
QAP	Quality Assurance Program
QOL	Quality of Life
RACGP	Royal Australian College of General Practice
RCPA	Royal College of Pathologists of Australasia
RCT	Randomised Controlled Trial
RE-LY	Randomised Evaluation of Long-Term Anticoagulation Therapy
ROCKET AF	Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared with Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation
SHPA	Society of Hospital Pharmacists of Australia
TE	Thromboembolism
TGA	Therapeutic Goods Administration
TIA	Transient Ischaemic Attack
TTO	Time Trade Off
TTR	Time in Therapeutic Range
UK	United Kingdom
USA	United States of America
VTE	Venous Thromboembolism
WHO	World Health Organisation

FOREWORD

Since it was first used in clinical practice over 50 years ago, warfarin has been plagued by complexities in its management. Over time, extensive experience with its use and technological advances has significantly improved the ease with which warfarin therapy can be managed. A range of healthcare providers have joined physicians in being responsible for care of patients on warfarin. In fact, patients themselves now have the ability to manage their own therapy if they wish. Despite these improvements, warfarin remains underused and sub-optimally managed in Australia.

Pharmacists, as a group of healthcare professionals, have been in search of a new professional direction for many years, probably since their role as compounder was significantly diminished with the technological changes of the early 20th century. Increased service delivery to improve chronic disease management is a role in need of considerable attention in contemporary society, and a role which pharmacists are ideally placed to fill. Enhanced anticoagulation service delivery is one area of chronic disease management that pharmacists have adopted internationally with impressive results.

This thesis aimed to examine the effect of using pharmacist-delivered models of care on warfarin management within Australia. To achieve this objective, a number of complementary projects were undertaken and form the structure of this thesis.

Part One seeks to explore the management of warfarin in the community. It provides an overview of warfarin therapy and the current models of management from the literature. There is a focus on the use of patient self-monitoring of warfarin therapy as a model of care and discussion on the impact of taking warfarin from a patient perspective. This Part also describes the potential areas for improving the management of warfarin and the roles pharmacists can play in the delivery of

chronic disease management services, such as anticoagulation management services.

Part Two explores the role for pharmacists in warfarin management. It describes a study titled *The Current State of Management of Australian Veterans taking Warfarin* which gives a snapshot of the level of anticoagulant control in an Australian community-dwelling veteran population. It goes on to describe a study of the *Development and Utilisation of an Online Anticoagulation Resource*. This project explored the role for pharmacists in improving patient education through web-delivered information. Part Two also describes the *Development and Implementation of a Flexible Anticoagulation Monitoring Service for Community Pharmacies*. This study was conducted as a small rural pilot project and a subsequent follow-up project. It describes the potential role for pharmacists to deliver enhanced anticoagulation services through community pharmacies, and the resources that were developed to support such service provision.

Part Three focuses on the role for pharmacists in facilitating patient self-monitoring of INR testing as a model of care in Australia. It describes a mixed methods study exploring the outcomes of patient self-monitoring of warfarin from both quantitative and qualitative perspectives. The quantitative aspect of the study, *Pharmacist-Based Model Enabling Patient Self-Monitoring of Warfarin*, incorporates two smaller patient groups which were subsequently combined to enable longer-term follow-up. Clinical outcomes and INR control are discussed from an objective perspective. The qualitative aspect of the study, *Exploration of Patient Views of Self-Monitoring of Warfarin*, reports the views of the self-monitoring participants and the subjective experiences of this model of care.

Part Four concludes the thesis with a discussion of the future of anticoagulation management in Australia. It discusses the potential role for pharmacist-delivered

services, focussing on those described in preceding Parts, and emerging pharmacological options in the area of anticoagulation.

Warfarin has been the mainstay of anticoagulation therapy for over half a century and may continue to play an important role for many years to come. This thesis explores the potential role for pharmacist-delivered anticoagulation services in an Australian context.

PART ONE: MANAGEMENT OF WARFARIN IN THE COMMUNITY

The management of warfarin in the community is often complex and impacted on by a vast range of external factors. This Part aims to give background, describing warfarin, the indications for its use and the current methods of managing warfarin therapy in community settings. There is a focus on the use of patient self-monitoring of warfarin therapy as a model of care and discussion on the impact of taking warfarin from a patient perspective. This Part also describes the potential areas for improving the management of warfarin and the roles pharmacists can play in improving outcomes for patients with chronic diseases, such as the delivery of anticoagulation management services.

Chapter 1 : A Brief Overview of Warfarin Therapy

1.1 Warfarin

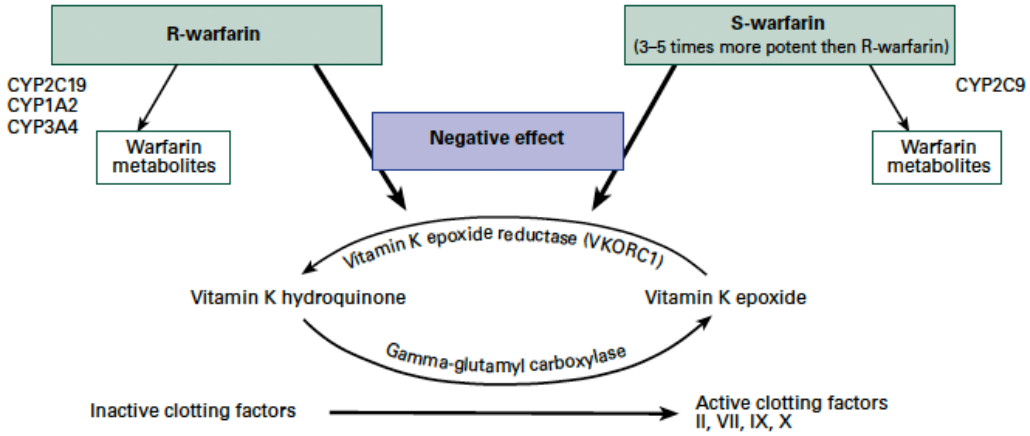
Anticoagulants are the drugs of choice for the prevention or treatment of venous thrombosis and cardioembolic events.[1] Their clinical effectiveness has been established in a variety of conditions. Oral anticoagulants are effective for primary and secondary prevention of venous thromboembolism (VTE), for prevention of systemic embolism in patients with prosthetic heart valves or atrial fibrillation (AF), for prevention of acute myocardial infarction (AMI) in patients with peripheral arterial disease, for prevention of stroke, recurrent infarction, or death in patients with AMI, and for the prevention of systemic embolism in high risk patients with mitral stenosis.[2-9]

Vitamin K antagonists have been in widespread use as the only oral anticoagulant agent available since the 1950s, and warfarin is currently the most commonly prescribed vitamin K antagonist worldwide.[10, 11] Despite the effectiveness of warfarin in a range of conditions, its use remains a challenge in clinical practice due to its narrow therapeutic window, the considerable variability exhibited in response between patients, the large number of drug and dietary interactions, and the complex dosing requirements.[12]

Vitamin K antagonists produce their anticoagulant effects by interfering with the cyclic conversion of vitamin K and vitamin K epoxide (Figure 1).[5] Vitamin K is a cofactor for the carboxylation of vitamin K-dependent proteins.[5] These proteins or coagulation factors, namely factors II, VII, IX and X, require carboxylation to produce their biological effect.[5] Vitamin K antagonists such as warfarin inhibit vitamin K epoxide reductase, preventing recycling of vitamin K and leading to partially carboxylated sub- or non-functional coagulation proteins.[13] Warfarin also inhibits

the carboxylation of the anticoagulant proteins C and S and so has the potential to exert a procoagulant effect, particularly early in therapy.[5]

Figure 1: Mechanism of action of warfarin



1.2 Complexities of warfarin treatment

Numerous obstacles exist to the safe and effective use of warfarin. Use is limited by the difficulty of managing therapy due to the requirement for frequent monitoring and the necessity for dose adjustments to limit the adverse consequences of a narrow therapeutic window, multiple food and drug interactions, and variability in pharmacodynamics and pharmacokinetics.[14]

The physiological activity of warfarin therapy is monitored by the International Normalised Ratio (INR), a standardised method of reporting prothrombin time (PT). The prothrombin time measures the level of the anticoagulation induced clotting defect in a sample of blood.[15] The PT of the sample of blood is compared to the mean normal PT, determined with fresh plasma samples from at least 20 healthy individuals of both genders over a range of ages, and is converted to the INR according to the level of activity of the thromboplastin used in the test.[5]

The activity of each thromboplastin is measured and assigned an International Sensitivity Index (ISI).

$$INR = (patient\ PT/mean\ normal\ PT)^{ISI}$$

Unexpected fluctuations of INR values present further challenges to therapy management and can be attributed to numerous factors including changes in diet, poor compliance with medication, alcohol consumption, and drug-drug interactions.[2, 16, 17]

Fluctuating levels of vitamin K in a patient's diet may influence their anticoagulant response to warfarin.[4]. Increased intake of vitamin K (from green leafy vegetables or supplements) will decrease the INR, resulting in an acquired resistance to warfarin.[18-20] A deficiency of vitamin K (from dietary deficiency, through drugs such as antibiotics which decrease bacterial production of vitamin K, or from states of fat malabsorption) results in a potentiated anticoagulant response and an increased risk of haemorrhage.[4, 21, 22]

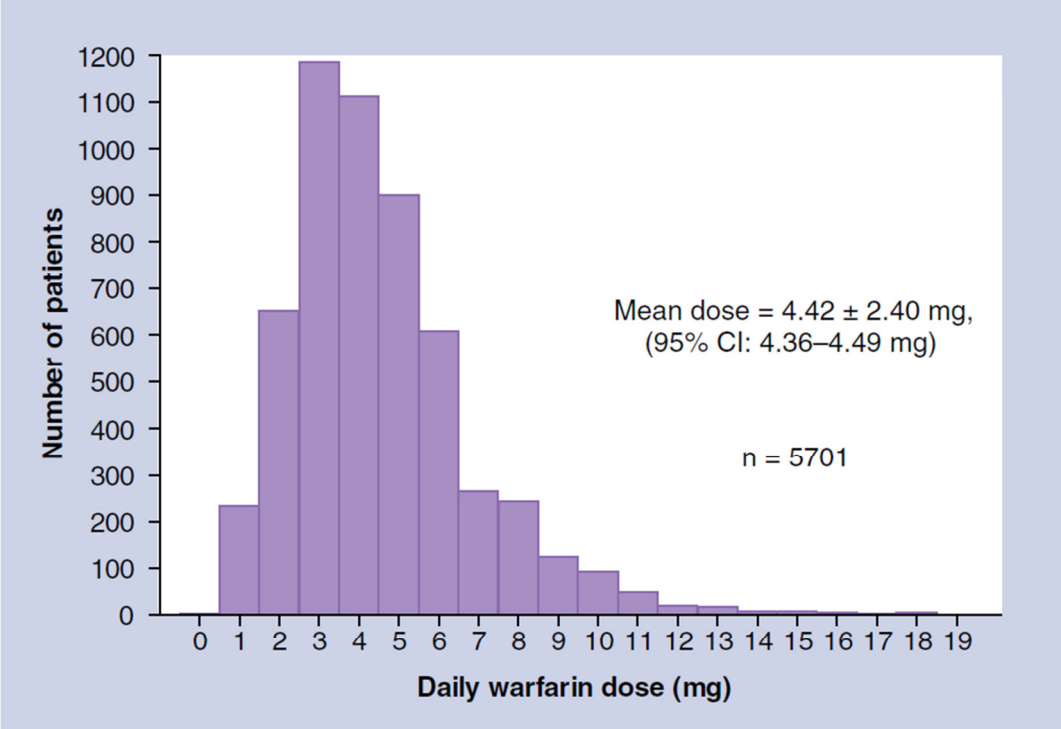
The dose-response relationship of warfarin may be influenced by both pharmacokinetic factors and pharmacodynamic factors.[2-4, 23, 24] The pharmacokinetics of warfarin may be altered by drugs which reduce its absorption from the small intestine or which affect its metabolic clearance.[4, 20, 25] The anticoagulant effect of warfarin is potentiated by drugs that inhibit its metabolic clearance,[4, 22, 26, 27] and reduced by drugs that increase its metabolic clearance, such as rifampicin and carbamazepine (Table 1).[2] Chronic consumption of alcohol may also increase the clearance of warfarin.[2, 22]

Table 1: Examples of agents which cause pharmacokinetic interactions with warfarin (adapted from Hirsh *et al.*[5])

Inducing agents *(increase metabolic clearance)*	**Inhibiting agents** *(reduce metabolic clearance)*
Barbiturates	Amiodarone
Carbamazepine	Metronidazole
Dicloxacillin	Omeprazole
Griseofulvin	Trimethoprim/sulfamethoxazole
Phenytoin	
Rifampicin	

The pharmacodynamics of warfarin are subject to genetic and environmental variability.[2] Hereditary resistance to warfarin occurs, where patients require up to 20-fold greater doses than average to achieve an anticoagulant effect (Figure 2).[2, 28] On the other hand, an exaggerated response to warfarin may be seen in elderly patients, thought to be due to a reduced clearance with age, or simply an increased sensitivity to anticoagulant effects.[2, 29, 30] It has been suggested that this heightened response is due to age itself, and not simply attributable to coexisting medical conditions.[29, 31] Genetically determined high responders to warfarin also exist and experience bleeding complications four times more commonly than other patients if this sensitivity is not recognised and appropriate dose reduction provided.[32]

Figure 2: Distribution of warfarin dose requirement at steady state (from Kurnik *et al.* 2009)[33]



Response to warfarin therapy may also be altered by herbal preparations which have the potential to cause pharmacokinetic or pharmacodynamics interactions. At least 60% of patients report using at least one complementary medicine on a regular basis,[34] however 60% of these patients do not report the use of alternative therapies to their healthcare providers.[25] This makes evaluating and managing warfarin interactions with herbal products an additional challenge

1.3 Complications of anticoagulant therapy

Despite its proven benefits in preventing thromboembolic conditions, warfarin is well recognised as a high-risk drug for adverse drug events.[35-42] It is frequently cited as a leading drug involved in preventable serious adverse drug events[43] and, in primary care, warfarin belongs to one of the classes of medicines most commonly associated with fatal medication errors.[44]

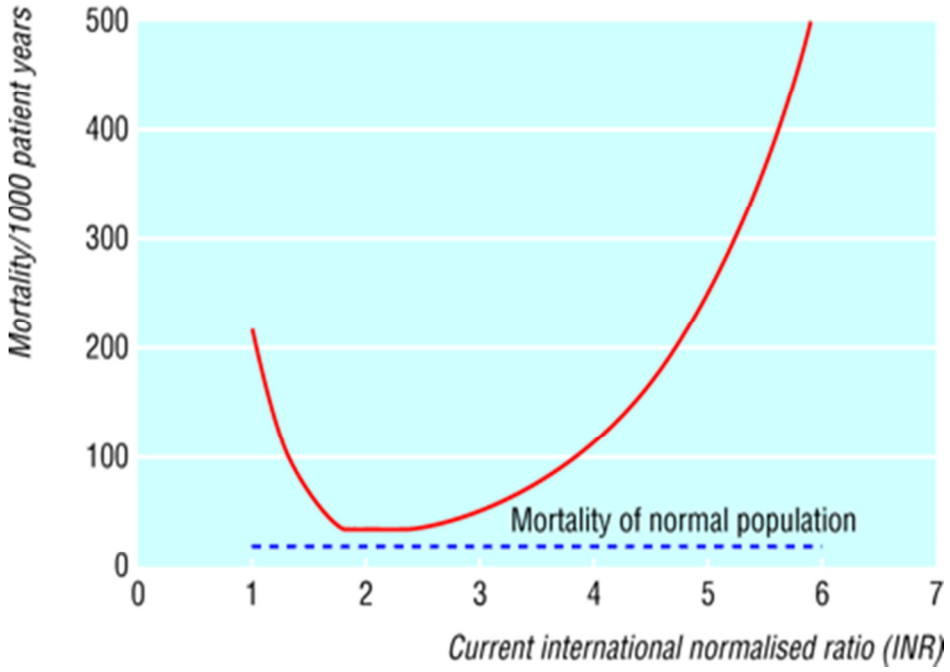
Not surprisingly, the major complication of anticoagulant therapy is bleeding.[45, 46] The average annual frequencies of fatal, major, and major or minor bleeding during long-term warfarin therapy are 0.6%, 3.0%, and 9.6%, respectively; these frequencies are approximately five times those expected without warfarin therapy.[45, 47] Major independent risk factors for bleeding during long-term warfarin therapy include co-morbid conditions other than the indication for therapy, history of stroke, history of gastrointestinal bleeding, advancing age (greater than 65 years), and the intensity of anticoagulant therapy.[45, 47-49]

The risk of these bleeding adverse events depends largely on the proportion of time during which the INR is outside the therapeutic range.[50] The aim of monitoring the INR is to maintain the INR within the therapeutic range, at an intensity of anticoagulation capable of preventing thromboembolic events without unacceptably increasing the risk of bleeding complications (Figure 3).[51, 52] The therapeutic range for warfarin is narrow and varies depending on the indication for use and patient characteristics.[12] For most indications, a moderate intensity target INR range of 2.0-3.0 is effective.[12] A higher target of 2.5-3.5 is recommended for patients with mechanical heart valves.[53]

Optimal management of anticoagulant therapy with warfarin is inextricably linked to the proportion of time that patients spend in their target INR range.[54] Time in therapeutic range (TTR) can be used to accurately predict both reductions in adverse event rates,[55] and clinical outcomes.[51] Despite the strong association between good control and outcomes of anticoagulation therapy, in well conducted clinical trials TTR is usually only 60% to 65%,[56-60] with some studies estimating that patients on warfarin may be in their therapeutic range as little as one-third of the time.[24] Ideally, a TTR of 100% should be the goal and would result in optimal clinical outcomes, however the literature suggests that high quality anticoagulation

management should aim for a TTR of at least 60-70%.[61, 62] TTR is closely correlated with clinical outcomes, and improvements in TTR of as little as 10% have been shown to convey a significant improvement in all-cause mortality.[54, 55, 63-65] Therefore, maintenance of the INR in the therapeutic range, and achievement of a high TTR, is the primary goal of warfarin management.[66]

Figure 3: Risk of death associated with different levels of anticoagulation (from Oden and Fahlen, 2002)[67]



To date, the largest published data on INR control in an Australian setting comes from the Point of Care Trial (PoCT).[68-70] This trial commenced in late 2005 and was designed to investigate the safety, clinical effectiveness, cost effectiveness and satisfaction of POC testing versus laboratory testing in a general practice environment for a number of POC tests, including INR. The trial recruited 944 patients taking warfarin from 58 practices spread across metropolitan, regional and remote Australia with a median age of 73 years.[70] INR results were available for 801 (84.9%) patients at baseline.[70] These baseline results could be used as an indication of the INR control of a cohort of Australian patients managed in a community-based

usual care environment. Unfortunately, the baseline results have been reported as the proportion of patients in range at the commencement of the study, or the point prevalence, rather than the time in therapeutic range, as is the gold standard of assessing INR control. At the commencement of the study, 513 (54.3%) of patients were within range, 188 (19.9%) were below the target range and 100 (10.6) were above the target range. Baseline data was missing for 143 (15.1%) patients.[70]

Of the 944 anticoagulated patients in the PoCT, 372 were recruited into the control group and undertook INR testing by pathology laboratories and dosing by their GP, or 'usual community-based care'. The intervention group underwent a 12 month phase of being tested by POC at their general practice.[70] At the conclusion of the trial, 372 (61.5%) of those patients in the control group were reported to be within their target range based on the point prevalence, or final INR result measured.[68] The proportion of tests with the target range for the control group was reported to be 57.6%.[68] The TTR of both the usual care and the intervention groups during the intervention phase of the PoCT trial was reported in post hoc analyses to be 68%.[71] Very little other published data is available on the INR control of the Australian population taking warfarin. One Australian study found the TTR of community managed patients to be 54%.[72] A small study of 26 indigenous Australians managed in remote Australia found a TTR of 44.9%,[73] while a study of 227 rural community-based patients managed by an anticoagulation clinic reported a TTR of 68.6%.[74] Further data would be useful to inform discussions on the future of warfarin therapy in Australia.

1.4 Optimal anticoagulant use

Poor control of warfarin therapy, particularly in the elderly, is a common cause of adverse drug reactions (ADRs) in Australia. Recent data shows that anticoagulants are one of the major causes of ADRs, and the rate of anticoagulation-related ADRs

has increased dramatically in recent years.[75] Optimal control of warfarin therapy is extremely important. It has been estimated that maintaining a high levels of INR control would prevent 1750 episodes of bleeding and 700 ischaemic strokes each year in Australia,[76] and could avoid one in every four haemorrhagic events, and one in every ten thromboembolic events experienced in elderly anticoagulated patients.[76]

It has been conclusively demonstrated in the literature that optimal anticoagulation therapy with warfarin can reduce the annual risk of stroke by approximately 68% in patients with non-valvular AF, making warfarin three times more effective than aspirin for stroke prevention in this population.[7, 77-84] However, much of this potential remains unfulfilled because of under and suboptimal use.[85] In elderly patients, who often possess multiple risk factors and are at higher baseline risk for stroke, the potential benefits of warfarin may be even greater.[86]

The presence of AF has been found to more than quadruple a person's risk of stroke[87, 88] and accounts for approximately 14% of all strokes in patients greater than 60 years old,[89] and 25% of strokes in those aged over 80 years.[86] Ischaemic strokes associated with AF are typically more severe than those which occur in the absence of AF, and this increased severity is independent of increasing age and other risk factors for stroke.[90] AF also significantly increases the risk of stroke recurrence after one year and increases post-stroke mortality at both 30 days and one year.[90, 91] Unsurprisingly, the increase in mortality and morbidity associated with AF translates to a significant cost to the healthcare system and the economy as a whole. In a report commissioned by the National Stroke Foundation, the Australian health system expenditure associated with strokes in the presence of AF in the 2008-2009 financial year was estimated to be $874 million, while the total cost to the Australian economy of these events was estimated to be at least $1.25 billion.[92]

Despite the demonstrated benefits of anticoagulation therapy in significantly reducing thromboembolic complications associated with AF, and the enormous cost savings that would result from optimal anticoagulant use, they remain underused.[93] A number of risk stratification tools exist for assigning a level of stroke risk to a person based on their medical history and conditions. One of these is the $CHADS_2$ risk assessment method, which awards one point each for congestive heart failure, hypertension, age >75 years, and diabetes mellitus.[94] Two points are given to a patient with prior stroke or TIA.[94] A patient at low risk for stroke would have a $CHADS_2$ score of 0 to 1, a patient at moderate risk would have a score of 2, and a patient at high risk would have a score of ≥3

Table 2).

Table 2: $CHADS_2$ risk stratification (adapted from Goldstein et al. 2006)[95]

$CHADS_2$ score	Risk level	Stroke rate (%/year)	Treatment recommendations based on risk stratification
0	Low	1.0	Aspirin*
1	Low-moderate	1.5	Warfarin** or aspirin*
2	Moderate	2.5	Warfarin**
3	High	5.0	Warfarin**
≥4	Very high	>7.0	Warfarin**

** 75-325mg per day*

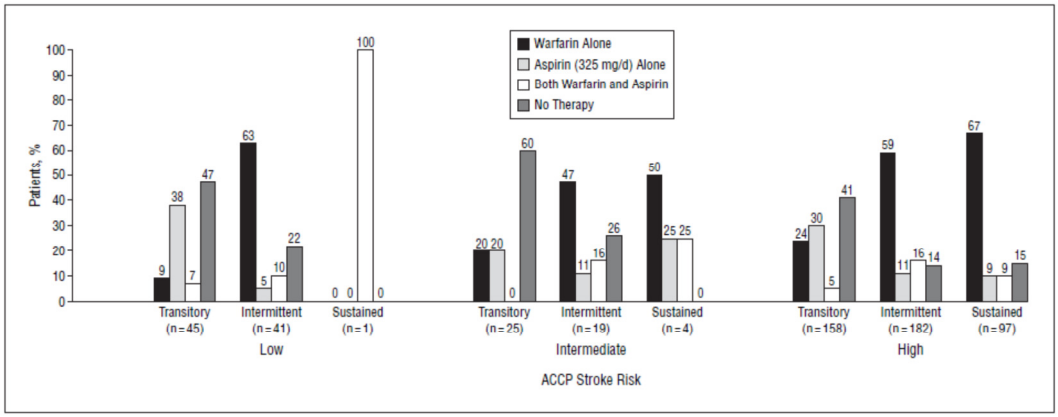
*** INR 2.0-3.0; consider patient preferences, bleeding risk, and access to INR monitoring*

A recent systematic review found that most of the included studies reported underuse of oral anticoagulants for high-risk AF patients.[93] They found that most studies based on the $CHADS_2$ score reported treatment levels of eligible patients classified at high risk (score of ≥3) of between 39% and 70%.[93] Data from the UK suggests that 50% of patients with AF who should be taking warfarin are not receiving it,[96] while data from the US suggests that only about one third of general practice visits for patients with AF included mention of vitamin K antagonists.[97]

While the structure of healthcare systems and funding models differs from country to country, it has been proposed that the reasons for underuse are widely applicable and include low levels of therapy initiation, the narrow therapeutic margin of available anticoagulants and the associated inconvenience of monitoring, patient compliance, and physicians' fear of bleeding events.[98-100]

In many instances, physicians appear to initiate anticoagulation and antithrombotic therapies based solely on their attitudes to therapy rather than the appropriate guidelines.[101, 102] One study found that anticoagulation is often initiated primarily on the classification of AF, rather than the calculated risk of stroke (Figure 4).[101] Glazer *et al*. found approximately three quarters of patients with newly detected AF received antithrombotic therapy (warfarin or aspirin) during the first six months of follow-up. However, 41% of patients at high risk of stroke did not receive warfarin despite guidelines recommending anticoagulation for such patients.[101] They found that AF classification was the strongest predictor of warfarin use (compared with transitory AF, the RR for intermittent AF was 2.8 [95% CI, 2.2-3.6], and the RR for sustained AF was 2.9 [95% CI, 2.2-3.7]), with none of the other stroke risk factors or warfarin contraindications being significantly associated with warfarin use.[101]

Figure 4: Use of antithrombotic therapy by AF classification and American College of Chest Physicians (ACCP) stroke risk (taken from Glazer *et al.*[101])



A systematic review by Pugh *et al*.[102] found that physicians are reluctant to recommend warfarin for elderly patients in AF, despite evidence supporting an increased benefit of warfarin in elderly patients compared with younger patients. Advancing age was found to be the most important barrier to the prescription of warfarin.[102] Bleeding risk and falls risk were also found to be disproportionate barriers to initiating warfarin therapy.[102]

Clearly, improvements are needed in the assessment of stroke and bleeding risk factors to enable warfarin to be prescribed safely and appropriately to all patients in whom it is indicated. A number of tools for stratifying both bleeding and stroke risk exist.[95, 103-107] However, the widespread application of these tools has been hampered by complex calculating methods, a lack of consensus and varying predictive values of some of the scores.[108]

The $CHADS_2$ scheme for categorising stroke risk for patients with AF (described above), recommends 'oral anticoagulation or aspirin' for people categorised at low-moderate risk ($CHADS_2$ score = 1).[95] However, recent data suggests that in patients with a $CHADS_2$ score of one, oral anticoagulation is superior to aspirin for stroke and mortality prevention.[109] The $CHADS_2$ score has many limitations and does not include some known risk factors for thromboembolism; as such it has recently evolved to a more refined risk stratification tool.[108] This tool is the CHA_2DS_2-VASc score (Table 3) which identifies low risk AF patients as those with a score of zero.[109] All other patients (CHA_2DS_2-VASc score ≥ 1) can be considered for antithrombotic therapy.[109] This consideration of whether to utilise antithrombotic therapy could be guided by the use of a bleeding risk stratification tool, rather than simply relying on the physician's perception of bleeding risk.[109] The HAS-BLED bleeding risk score (Table 3) is one such simple tool which assigns points for bleeding risk factors and has the potential to support clinical decision making in patients with AF.[103] A HAS-

BLED score of 0-2 would suggest the patient is at a low bleeding risk, while a score of ≥3 would suggest a risk of bleeding that would warrant consideration.[108]

Table 3: Risk stratification with CHA_2DS_2-VASc and HAS-BLED scoring schemes (based on data from Lip *et al.*[109] and Pisters *et al.*[103])

CHA_2DS_2-VASc Acronym	**Score**	**HAS-BLED Acronym**	**Score**
Congestive heart failure/left ventricular dysfunction	1	**Hypertension**	1
Hypertension	1	Abnormal renal and liver function (1 point each)	1 or 2
Aged ≥ 75 years	2	**Stroke**	1
Diabetes mellitus	1	Bleeding	1
Stroke/TIA/TE	2	Labile INRs*	1
Vascular disease (prior MI, PAD, or aortic plaque)	1	**Elderly**	1
Aged 64-75 years	1	Drugs or alcohol (1 point each)	1 or 2
Sex (female category)	1		
Maximum score	*10*	*Maximum score*	*9*

** Labile INRs refers to unstable/high INRs or poor TTR*

When comparing the two risk stratification tools it becomes clear that there are a number of risk factors for stroke which are also risk factors for bleeding (shown in bold in Table 3).[110] This becomes particularly important when the use of anticoagulants in the elderly is considered, and the overlap of potential risk versus benefit in this population.

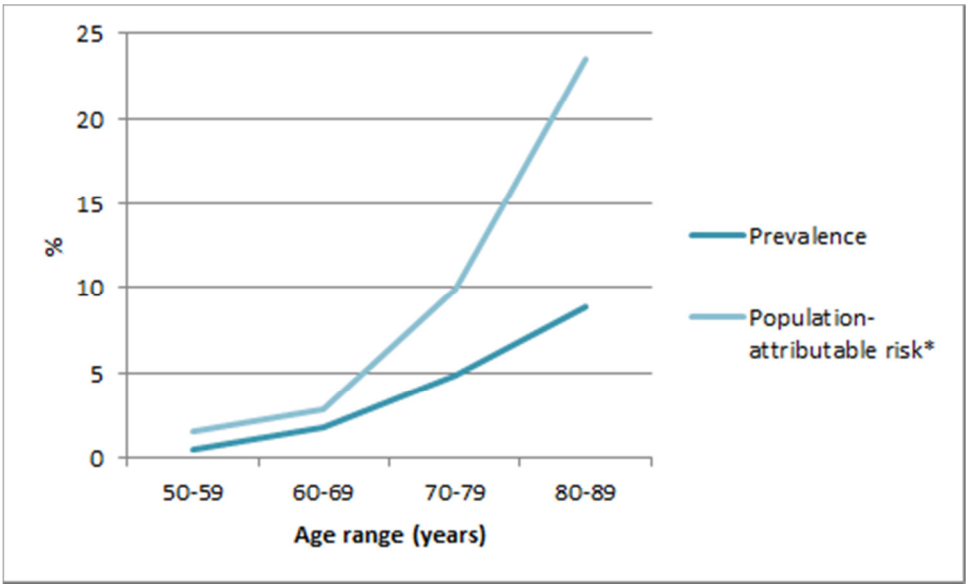
1.5 Warfarin use in the elderly

Elderly patients with non-valvular AF and acute or recurrent VTE account for a large proportion of people receiving anticoagulant therapy.[111, 112] Anticoagulation in the elderly poses additional challenges because these patients are simultaneously at higher risk for recurrent thromboembolism and for major bleeding, including intracranial haemorrhage. [46, 113, 114]

Elderly people are particularly vulnerable to stroke when AF is present, with the risk of stroke attributable to AF rising from 1.5% for those aged 50-59 years to

23.5% for those aged 80-89 years (Figure 5).[87] At the same time, bleeding complications with anticoagulant drugs appear to occur more frequently in older patients than in younger individuals.[45, 48, 113-118] In addition to age-related sensitivity,[29] older patients may be at an increased risk for anticoagulant-related bleeding because they generally have an increased incidence of ADRs, increased prevalence of comorbidities and polypharmacy, and increased vascular and endothelial fragility.[119]

Figure 5: Age as a risk factor for stroke in patients with AF (based on data from Goldstein *et al*. 2006)[95]



* *Population-attributable risk is the proportion of ischaemic stroke in the population that can be attributed to a particular risk factor, in this instance AF.*

A meta-analysis clearly demonstrated that age does increase the risk of serious anticoagulant associated bleeding.[118] However, it also demonstrated that the risk of serious haemorrhage due to oral anticoagulants was far smaller than the beneficial reduction in stroke risk for patients with AF.[118] The authors concluded that the absolute benefits of oral anticoagulants actually increase as patients get older and their risk of stroke increases.[118] Despite the benefits, physicians remain hesitant to prescribe anticoagulants to elderly patients, citing a fear of haemorrhage, a

perceived lack of efficacy and a difficulty with compliance with INR monitoring in this patient group.[120]

1.6 An increasing demand for anticoagulants

While remaining under prescribed for stroke prevention in AF, awareness of appropriate stroke prophylaxis is improving and the use of anticoagulants overall is actually increasing. It is estimated that the use of warfarin around the world is now increasing at a rate of approximately 10% per year;[10, 115] the use of warfarin in Australia has also been increasing at approximately 8% to 10% per year over the past decade.[121] This increase is particularly apparent in elderly patients, because of warfarin's proven benefits in AF and the increasing prevalence of this condition.[10, 35, 77, 122-124] The prevalence of AF rises with age, with approximately 10% of people over the age of 80 years being affected.[111] Increasing numbers of elderly patients are candidates for, and could benefit from, the use of anticoagulants.[125] The increasing age of the population is expected to result in current demand for oral anticoagulant therapy increasing up to six-fold by 2050.[126] Other reasons for the increasing use of anticoagulants include increasing common disease indications for their use, and improvements in anticoagulant safety and management methods.[24]

Chapter 2 : Warfarin Management in the Community

Achieving quality control of warfarin therapy can be difficult as it requires frequent blood samples and trips to the site of usual care testing.[127] Hence, maintaining the INR within the target range is often a time-consuming process for physicians and patients and has been cited as one reason for non-prescription of warfarin.[128] This process can reduce patient compliance and increase the risks associated with treatment,[129] especially in people who are housebound, live far from a monitoring site, or who have a regular job and find it difficult to attend regular appointments.[130]

2.1 Education

Successful anticoagulation treatment is dependent on the patient's knowledge of warfarin,[131] and there is a generalised acceptance in the medical literature that patients who have a good understanding of warfarin therapy will experience fewer complications with therapy.[132] Knowledge, drug compliance, and anticoagulation control all improve after patient education becomes part of the management plan.[133-136] However, it is important to ensure that the education being delivered is of a high standard, targeted to the individual patient and their situation, and comprises more than simply the passing on of information. Low quality education has actually been found to be more devastating and associated with higher rates of bleeding than those associated with a complete lack of education.[137]

Recent studies have shown that patient knowledge of warfarin in a community setting is often poor.[138-142] Studies have generally shown an inverse relationship between patient knowledge and adverse outcomes of warfarin therapy, primarily major bleeding.[84, 136] Positive outcomes have been recorded where patients have had increased participation in their care and where they were encouraged to communicate more effectively with doctors and other health professionals about drug interactions and changes in lifestyle or diet.[136] This is likely to be because

knowledge has been cited as a strong determinant of anticoagulation control.[141] Kagansky *et al.*[137] evaluated risk factors for bleeding among older patients on warfarin and found insufficient education to be a major factor predicting bleeding episodes. Patient education regarding anticoagulation therapy and patient empowerment are therefore important elements in improving quality of treatment and patient awareness, and could also be a major factor for improving patient compliance.[143]

Compliance with warfarin is essential to maintaining good anticoagulant control and to preventing unnecessary dosage changes.[144] The IN-RANGE study utilised electronic medication bottle caps to determine the effect of adherence on anticoagulation control. They found significant associations between both under adherence (defined as missed pill bottle openings) and under anticoagulation and extra pill bottle openings and over anticoagulation.[144] They concluded that poor compliance has a significant effect on anticoagulation control.[144] The study also found that compliance to warfarin regimens changes over the course of treatment and that patients may benefit from ongoing counselling throughout treatment to improve their compliance.[145]

Barcellona *et al.*[146] also linked the level of knowledge to compliance. They found patients who stated they sometimes missed a daily dose of their anticoagulant did not understand the need to take the therapy every single day and as such spent substantially less time within their therapeutic range.[146] They concluded that greater emphasis should be given to educational courses for anticoagulation patients in an attempt to improve knowledge levels, and in turn improve compliance.[146] Other studies have also identified a lack of patient knowledge regarding the important aspects of warfarin therapy as a determinant of non-adherence to therapy.[147]

In addition to increasing compliance, education has also been attributed to reducing adverse events during warfarin treatment.[137, 141, 148] The risk of bleeding due to warfarin therapy is closely related to the adequacy of warfarin control.[149-151] Written and verbal education has been shown to improve control of the level of anticoagulation in a number of studies.[136, 141, 152] Roddie and Pollock[133] showed that 85% of patients with a good understanding of warfarin had a well-controlled and stable INR, compared to only 63% in the poor-understanding group. Generally, patients' knowledge, therapy compliance and anticoagulant control all improve after patient education becomes part of a structured management program.[133, 135, 136, 153]

Successful, safe anticoagulation depends on patient education, good compliance and communication with the patient and between health professionals responsible for their clinical care.[44] The rate of warfarin-related hospitalisation for bleeding is substantially lower for patients who reported receiving medication instructions from a physician, nurse or pharmacist;[154] however, literature reports the quality of the provision of educational materials to hospitalised patients started on warfarin is generally poor.[155] Improving patient knowledge may improve control, reduce complications and therefore reduce the burden on health services.[156] General practitioners (GPs) and community pharmacists should play a key role in reinforcing knowledge regarding anticoagulation to reduce the risk of complications of anticoagulant therapy. Warfarin training should be tailored to suit the level of education and the age of the patient;[72, 141, 157] education of elderly and illiterate patients in particular may require special consideration and may need to include the use of visual aids.[141]

2.2 Improving access to educational resources

Warfarin is a complex medication to manage for both health professionals and patients. Appropriate patient education and high levels of knowledge of warfarin

therapy are necessary to maximise patient safety and clinical outcomes while taking this medication.[131] Factors which may impact on the efficacy of warfarin include diet, alcohol intake, concurrent medication use, illness and adherence.[158] While these factors are usually discussed with patients during counselling on initiation of therapy patients often misunderstand or cannot recall all of the information with which they are provided.[159] A lack of structured and ongoing education has been identified as an issue for people of all ages with many chronic conditions, including those taking warfarin.[160-162]

One model for providing ongoing patient education in healthcare involves the use of internet-based educational approaches. Studies estimate between 44-58% of people use the internet to search for medical information.[163-165] Computer-based education has been described as an effective strategy for increasing health knowledge and the adoption of healthy behaviours.[166-168] It has benefits in providing education to hard to reach patients,[169] and for patients needing to confront difficult or daunting health issues.[168] Computer-based education provides information that is available at a time convenient to patients, which can be learnt in a private and comfortable environment and which allows immediate reinforcement of learning.[167] Given that warfarin is usually a long-term and often a life-long medication, the relative complexity of its dosing and monitoring requirements, and the seriousness of both its adverse effects and the medical conditions it is used to treat, these benefits make computer-based education a particularly relevant tool for people taking warfarin.

While the availability of reliable online information is an important first step, it is also necessary to ensure that the information presented can be easily navigated and interpreted by the intended audience. Usability of websites needs to be taken into consideration to ensure the audience can navigate the site and access the

information[170]. This is an especially important consideration for the warfarin-taking population, as they are generally older and likely to have less experience using the internet than the general population.

In addition to presenting information in a usable format, it must also be accessible to people with a wide range of health literacy levels. Health literacy has been defined as "the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions".[171] The impact of literacy on health is significant,[172] and overall general literacy levels may impact an individual's health literacy, however it is not the only factor that is important. Health literacy is a concept related to an individual's education level, age, geographic location, income and ethnicity.[173] Studies have demonstrated that low levels of health literacy are associated with worse health status and high rates of hospitalisation,[172, 174-177] and that the elderly are likely to have even lower health literacy levels than the general population.[172, 178-181] Ageing causes an increasing dependence on health care services, which in turn requires the ability to interact and communicate with health services and a reasonable level of health literacy.[182] Unfortunately, in Australia 83% of those aged 65 to 74 years did not achieve the minimum level of health literacy regarded as that required to meet the complex demands of everyday life.[182]

While health literacy is hard to predict and is very individual,[183] one method which can be used to attempt to improve comprehension of health information is to ensure the readability of information is targeted at an appropriate level. Readability can be determined using a variety of formulas, including the Flesch-Kincaid Grade Level[184] and the Simple Measure Of Gobbledygook.[185] These assess the number of syllables per word and, in the case of Flesch-Kincaid, the number of words per sentence, and assign a level of reading difficulty.[184, 185] The lower the reading grade assigned, the

greater the readability of the information. Recommendations suggest that patient health information be targeted at a Flesch-Kincaid reading level of 6th to 8th grade.[186] Unfortunately, much health information currently published is beyond the comprehension skills of the general population.[173, 187]

While the volume of patient-centred health information on the internet has grown in recent years,[188] there is a lack of quality, patient-focussed information on warfarin. Searching commonly used internet search engines results in identification of only a small number of warfarin-related websites, and even fewer which provide patient-focussed information. Of those which do provide patient information, many are complex to navigate and the information contained on them is often above the recommended reading level.[189] Improving the quality and accessibility of web-based warfarin information may be an important step in improving the outcomes of people taking anticoagulants.

2.3 Methods of monitoring

The majority of people taking warfarin in Australia are currently managed in traditional general practice settings. This management process often involves frequent collection of venous blood samples and visits to the doctor's practice or pathology laboratory. There has been concern over the standardisation of laboratories and the problems with patient-physician communication inherent in this process.[190, 191] The usual care process is labour intensive for the physician and the patient, respectively, as it requires two separate interactions with each monitoring event.[129, 190] The need for regular laboratory visits and subsequent follow up for dose adjustment is inconvenient and causes many patients to feel an unwanted dependence on healthcare practitioners.[192]

Recently, portable monitors capable of INR monitoring, such as the CoaguChek®XS (Figure 6), have become available. Traditional testing methods require venous

access, a relatively large volume of blood, and the time until a result is known may be several hours.[129] On the other hand, portable monitors can measure INR values from a capillary finger stick sample with results available in minutes.[190, 192] They are simple to use and their accuracy and reliability in a number of settings, including in the hands of patients, has been well documented.[127, 192-198]

Figure 6: CoaguChek®XS INR monitoring device (Roche Diagnostics)

The development of accurate and reliable portable monitors has enabled the widespread introduction of point of care (POC) testing of the INR. The key objective of POC testing of any physiological variable is "to generate a result quickly so that appropriate treatment can be implemented, leading to an improved clinical or economic outcome."[199] Rapid provision of results has been suggested to facilitate better clinical decision making, improve patient adherence and satisfaction, and improve clinical outcomes.[199] This holds true for the monitoring of patients taking

warfarin. Point of care INR testing devices have been shown to have the potential to minimise hospital and primary care visits for blood sampling and provide closer monitoring with less discomfort for the patient, improving overall quality of life.[200]

2.4 Models of management

A number of models of anticoagulation management are currently used in the care of patients taking warfarin. The three most commonly encountered models are traditional physician office-based management, anticoagulation clinic models, which may be conducted in a number of settings, and patient self-testing.[12]

2.4.1 Office-based management

Office-based management is often referred to as usual care or traditional care. It has been defined in some countries as "management by a patient's own physician with no staff spending 50% or more of their time on managing anticoagulation."[201] Traditionally, it has involved the patient visiting their physician's office or a pathology collection centre to have a venous blood sample drawn. This sample is then analysed at a pathology laboratory. INR results are communicated to the physician who communicates any subsequent dose adjustment to the patient, either by a telephone consultation or by a follow-up face to face consultation. This process is fraught with opportunities for error and suboptimal management. Laboratory results are generally not available at the time the patient sees the physician, there may be inadequate record keeping systems in place meaning doctors are sometimes unaware of the availability of INR results and histories, and communication systems are also described as often inadequate causing dosage adjustments to be provided to the patient late, or sometimes not at all.[202] Often, general physicians have relatively few patients on anticoagulant therapy and have little incentive to develop more efficient management systems.[202]

Despite these disadvantages, one Australian study found that the INR control and complication rate of unselected patients managed in the community by their local GPs was comparable to the literature of the time.[72] The study found that around 54% of patient time was spent within an INR range of 2.0-2.9. Another recent Australian study also found, at baseline, that only around 54% of patients were within their target range.[71]. While similar to two European trials,[203, 204] this level of control is well below that recommended for quality anticoagulation management.[62]

The availability of POC testing devices has changed the method of usual care for many patients. Point of care testing not only provides an alternative to pathology testing, but also allows a different style of patient management, compared with traditional pathology testing.[68] Physicians now have the ability to test the INR while the patient is in the clinic, enabling immediate communication of any dosage adjustments. This removes many of the complexities and multiple contacts required in the traditional usual care model. It also takes usual care a step closer to the systematic and coordinated care that has long been offered by anticoagulation clinics.

2.4.2 Anticoagulation clinics

Anticoagulation clinics may take the form of hospital outpatient clinics or specialised community-based clinics. In general, anticoagulation clinics can be defined as "a specialised program of patient management focused predominantly, if not exclusively, on managing oral anticoagulation."[205] Anticoagulation clinics are regarded as a more systematic and coordinated model of care than traditional office-based management.[12] They incorporate patient education, systematic INR testing, tracking and follow-up, and good communication with the patient regarding results and dosage decisions.[12] They also have the advantage of having the INR result

available whilst the patient is present, allowing for immediate dosage advice and additional education where necessary.

An anticoagulation clinic program is often directed by a single physician who assumes no responsibility for the primary care of the patients under their management, while the actual management is usually conducted by registered nurses or pharmacists, who become responsible for making dosage changes, scheduling future tests and providing education.[202, 205] The health professional assuming responsibility for the anticoagulation management then becomes an expert in the area and subsequently is able to offer an improved quality of care.[202] Both anticoagulant nurses and pharmacists have been found to be at least as safe and effective as physicians in managing anticoagulated patients.[206-210]

Anticoagulation clinics have been shown to be an effective way of improving the quality of anticoagulation management compared to usual care.[201, 202, 211-214] Studies consistently find clinically important differences in the TTRs achieved by anticoagulation clinics when compared to usual models of care.[201, 213-216] They also find that anticoagulation clinics achieve significantly lower rates of adverse clinical events in terms of both major haemorrhage and thrombotic events than are achieved with traditional care models.[209, 214, 216, 217]

Despite the improved outcomes that can be expected with clinic-based care, a considerable time commitment can still be required from the patient. Traditionally, patients had a venous sample drawn on arrival to the clinic and waited until the result was available before having their consultation. One study estimated that the time involved in attending an anticoagulation clinic could range from 42 minutes to 3.5 hours.[218] The increasing availability and adoption of POC testing devices has reduced the time involved in attending clinics and will continue to improve anticoagulation clinics' abilities to provide timely dose adjustments and education.

In a systematic review of 67 studies, involving over 50,000 patients, management by anticoagulation clinics was compared to usual community care.[56] It was found that time spent within the therapeutic range was generally lower in patients from community-based studies than in those from anticoagulation clinics, with mean TTRs of 50.0% (95% CI: 45.1-55.0%) and 65.6% (95% CI: 63.7-67.7%) respectively.[56] It was concluded that patients managed by community practices showed significantly worse anticoagulation control than those managed by anticoagulation clinics.[56]

Other systematic reviews have supported the suggestion that anticoagulation clinics offer improved control of therapy when compared to usual care.[219, 220] Anticoagulation clinics were found to be superior to usual care by Dolan *et al.*, resulting in improvements in time in range of 11.3% (95% CI: 0.1-21.7%).[219] Similarly, Cios *et al.* found that usual care resulted in a time in range that was 13.0% (95% CI: 7.9-18.0%) less than that achieved by specialist clinics.[220]

Another, more recent, systematic review identified three randomised controlled trials and eight cohort studies for review.[221] It was concluded that evidence for the safety and efficacy of anticoagulation clinics is limited but overall suggests that care provided by such clinics may lead to improvements in time in therapeutic range.[221] The analyses suggest that face to face interactions, computer-based monitoring systems for appointments, specialised staff, and the provision of written instructions have an important role to play in the improved care offered by anticoagulation clinics.[221]

2.4.2.1 Computer-assisted dosage support

While anticoagulation clinics alone have been shown to improve anticoagulation control, superior INR control is achieved by experienced personnel in anticoagulation clinics who utilise computer-assisted dosage adjustment

methods.[222] Computer-based dose adjustment programs typically calculate whether a dose adjustment is necessary from a pre-defined table of rules for the therapeutic range.[12] If the computer recommends a dose adjustment, it then uses the current INR and the target INR to calculate the new dose.[12] It is also able to calculate the time to the next test by taking into consideration the current INR, the interval which has passed since the last test, the number of previous dose changes, and the number of previous INR results in range.[12]

Numerous studies support the use of computer-based dosing algorithms over manual dosing methods.[223-227] They found that computer-based dosing gave better INR control, as measured by improvements in the TTR, when compared to manual dose adjustments made by expert medical staff.[223-227] Increases in TTR as great as 12% were seen through the use of computer-based dosing.[227] Other benefits reported include fewer extreme low results and fewer extreme high INRs,[226] and a reduction in adverse clinical events.[227] Computer-based dosing methods have also been shown to be at least as effective as physicians for the initiation of warfarin therapy, as well as for the long term management.[228, 229]

These positive findings in support of computer-based dosing algorithms have resulted in their widespread use in anticoagulation clinic situations and their inclusion in clinical practice guidelines.[230]

2.4.3 Patient self-testing

The availability of accurate, easy to use POC INR devices has led to the evolution of another model of anticoagulation management – patient self-testing. Patient self-testing can take the form of both patient self-monitoring and patient self-management. Self-monitoring involves the patient using the portable device to measure their INR result and communicating that result to a healthcare provider for dosage adjustment. Self-management takes the concept one step further, with the

patient both obtaining their own result and deciding on their dose adjustment, usually with the guidance of a predetermined dosing algorithm.

Patient self-testing is not a new concept, having been first described almost 40 years ago,[231] and substantial literature exists supporting the implementation of self-testing as a model of care.[232, 233] [200, 234, 235] Self-testing provides both patient-related benefits and clinical benefits and is associated with measures of INR control that are at least equivalent, if not superior, to those achieved by high quality anticoagulation clinics.[149, 236, 237] It provides potential for increased convenience, increased frequency of testing, increased knowledge and awareness of therapy and improved compliance.[12, 238] Several systematic reviews and meta-analyses have shown improvements in TTR and reductions in adverse events arising through patient self-testing.[200, 233-235, 239] Despite these benefits, anticoagulation guidelines historically have not endorsed self-monitoring or self-management.[240]

While not a management model necessarily suited to all patients on warfarin,[233] patient self-testing offers many benefits over conventional care for suitable patients. The adoption of patient self-testing of warfarin therapy to achieve appropriate outpatient anticoagulation and prevent complications was ranked in the top 10 clear opportunities to improve patient safety in a report prepared by the US Agency for Healthcare Research and Quality.[241] Despite this recommendation being made over 10 years ago, self-testing is not a model which is currently commonly practiced in Australia, yet it is one which deserves greater attention for wider implementation to improve anticoagulation management.

2.4.3.1 Patient self-monitoring

Patient self-monitoring of warfarin therapy involves a patient (or carer) performing an INR measurement and reporting the results to a healthcare provider who decides an appropriate warfarin dose and the timing of the next INR measurement.[242] Self-

monitoring allows the rapid provision of results which can facilitate better clinical decision making, improved patient adherence, and greater patient satisfaction with healthcare, all of which lead to improved clinical outcomes.[199] Patients with diabetes have been self-monitoring and self-managing their insulin therapy for decades.[129, 243] Warfarin monitoring is not as intense as blood glucose monitoring, but still requires frequent assessment of the INR to ensure safe and effective therapy.[128]

PSM is currently not well established in Australia, despite accurate and easy to use portable INR monitors having been readily availability for a number of years.[244] It has been suggested that the absence of mention of PSM as a management strategy in best practice guidelines on warfarin management may be a contributing factor to the lack of uptake of PSM in Australia.[233] However, recent guidelines do acknowledge the benefits of PSM for suitable patients,[12] and guidelines even exist specifically relating to the implementation of PSM and self-management.[65, 143]

Another factor which has been suggested to be likely to be significantly impacting on the current uptake of PSM in the Australian healthcare setting is the structure of the health system itself. PSM is currently not remunerated in any form by the Australian healthcare system, while pathology-based INR testing and visits to GPs are usually subsidised through Medicare, leaving the patient with little or no out of pocket expense. This payment structure is in stark contrast to that in place in many countries, and is potentially a major contributing factor to the minimal number of patients undertaking PSM in this country. The reasons underpinning the lack of financial support for PSM through the Australian public health system are yet to be understood, though formal cost-effectiveness analyses are certainly lacking in this setting.

Internationally, the situation relating to PSM is very different to that seen in Australia. Studies have been published arising from the USA,[190, 237] UK,[245, 246]

Germany,[191, 247] the Netherlands,[149, 248] Denmark,[249] and Italy,[130] supporting the introduction of PSM. In fact, PSM now forms part of the usual care model in many of these countries.

In Germany, there is a formalised and approved training program for patients to enable PSM, and The Association of Self-Management of Anticoagulation has established many training centres to train the doctors and nurses who will train patients.[65] It is estimated that at least 400,000 patients manage their own warfarin therapy in Germany alone.[65]

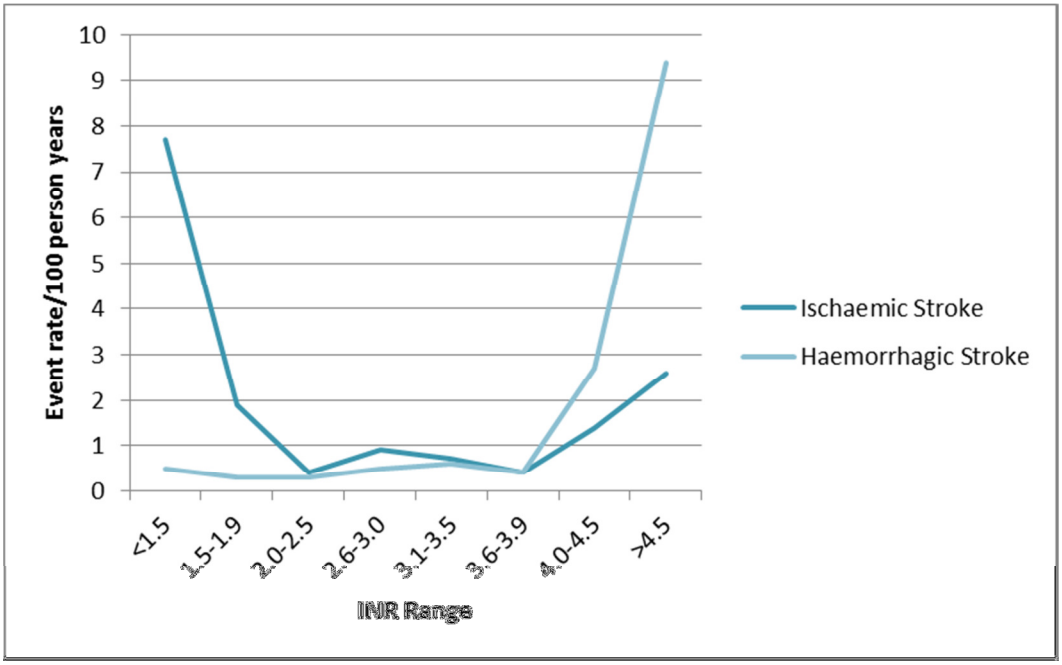
In contrast to Australia, many countries have opted to cover some or all of the costs associated with PSM through their healthcare model. In Germany and Denmark, patients have all expenses associated with PSM reimbursed, including the monitor and the test strips.[239] In the UK and Sweden, test strips are available on prescription and covered by the healthcare system, while the patients cover the cost of the monitor themselves.[239] In the USA, Medicare and most major insurance companies cover the costs of home monitoring for the most common indications for warfarin.[250]

The cost-effectiveness of PSM has been studied in a number of international healthcare settings. One study in the USA found that the cost of home-monitoring was approximately half that of routine care over an eight-week period, with costs based on the cost of monitor and test strips compared to the cost of hospital laboratory testing.[192] The authors felt that if improved control could be achieved through PSM, hence reducing the risk of thromboembolic and haemorrhagic complications, the cost savings associated with PSM would be substantial.[192] A Canadian study also found PSM a cost-effective strategy for those receiving long-term oral anticoagulation therapy for AF or for mechanical heart valve thromboprophylaxis.[251] A further study arising from Germany also found PSM to be cost-effective, with a 50% reduction in healthcare costs associated with PSM

compared to those associated with usual care.[238] Such cost-effectiveness data is lacking in the Australian context.

The expansion of PSM as a strategy worldwide for the management of oral anticoagulation can be largely attributed to the increasing number of patients on warfarin, and concerns over the ability of conventional healthcare services to cope with the corresponding increase in workload.[136, 191, 205, 252] PSM of anticoagulation is primarily based upon the premise that more frequent testing will lead to tighter anticoagulation control and thus improved clinical outcomes.[51] Data indicates that the mortality of patients taking warfarin is related to control of the INR; that is, an INR range of 2-3 is associated with the lowest rate of mortality for most indications.[67] Increasing rates of mortality are equally associated with both under- and over-anticoagulation (Figure 7).[67] It has also been shown that the time in the therapeutic range correlates strongly with clinical outcomes, both bleeding and thromboembolic, and that more frequent INR testing increases the time spent within this range.[51]

Figure 7: Annual event rates of ischaemic stroke and intracranial haemorrhage among patients with non-valvular AF who were taking warfarin, according to the INR at the time of stroke (based on data from Hylek et al. 2003)[63]



2.4.3.1.1 Benefits of self-monitoring

Warfarin therapy in Australia could be optimised through the introduction of new strategies, such as PSM, which have been implemented elsewhere in the world and have been demonstrated to improve clinical outcomes, patient satisfaction and quality of life.[130, 237, 248, 249]

The concept of PSM with dose-adjustment of anticoagulation based on physician-derived guidelines, referred to as patient self-management, was first tested in 1974 by Erdman *et al.* in patients with prosthetic heart valves.[231] Even at this early time, self-managed patients demonstrated a greater degree of satisfactory anticoagulation control (95%) compared to a retrospective survey of standard patients who achieved only 71% adequate anticoagulation.

Since Erdman's original study, a large number of studies have examined the benefits of PSM, with and without patient managed dose adjustment, in a variety of study

settings. Ansell *et al.* analysed the results of PSM with dose-adjustment over seven years with 20 patients.[190, 253] These patients performed their own INR testing and adjusted their own warfarin dose based on physician guidelines. The results from this group were compared with a matched group being treated by an anticoagulation clinic. The self-managed patients were found to be in the therapeutic range for around 89% of the determinations, compared to 68% for those managed by the clinic. They also found the study group had fewer dosage changes (11% vs. 28%) and that complication rates did not differ between the groups. Patient satisfaction with this model of therapy was reported to be very high.

Siebenhofer *et al.* conducted a systematic review of studies of self-management of oral anticoagulation, evaluating randomised controlled trials from 1966 to 2003.[234] The studies included in the review showed that self-management can improve the quality of oral anticoagulation therapy.[234] This was demonstrated by an increased number of INR values in the target range and a reduction in the risk of thromboembolism and bleeding complications. Self-management of oral anticoagulation was found by these studies to be safe, improving patient satisfaction and treatment-related quality of life.[234]

Sawicki *et al*. assessed the effects of PSM with dose-adjustment over a five year period and demonstrated that the improvements in INR control and quality of life were sustained with long-term self-management. One hundred and seventy-eight patients were trained to perform self-management, with the initial study showing improvements in the quality of anticoagulation control.[191] These improvements were sustained to five years.[254] Similarly, at five years, improvements were also retained in patient quality of life measure when compared to baseline.[254] At baseline, 29% of INR values were within the target range, with a squared INR deviation of 1.32. This was increased to 53% of results within the target range, and

a drop in the squared INR deviation to 0.65, for the intervention group of the initial study. After five years, 62% of results were in range, with a further drop in the squared INR deviation to 0.44, suggesting that not only is the improvement in INR control after participation in a self-management program long-lasting, the quality of anticoagulation control may even increase further with increasing duration of self-management.[254]

The results of Siebenhofer's systematic review were complemented by the establishment of the long-term survival benefits of patients performing self-management.[255] In a follow-up study of the Early Self-Controlled Anticoagulation Trial, 930 patients were followed for up to 12 years following the initial study.[255] According to both intention to treat analysis and per protocol analysis, the self-management group was associated with a 10-year improved survival of 23% (95% CI 0.58-1.0) and 33% (95% CI 0.51-0.89), respectively, compared to patients in the usual care group.

Further support for PSM arose from a 12-month trial in the UK by Fitzmaurice *et al*., published following the systematic review, where 617 patients receiving warfarin were randomised to intervention (self-monitoring of INR twice a week and a simple dosing chart to interpret the dose of warfarin) or routine care.[256] No significant differences were found in the TTR between self-management and routine care (70% vs. 68%). However, self-managed patients with poor control before the study showed an improvement in control that was not seen in the routine care group. It was concluded that with appropriate training, self-management is safe and reliable for a sizeable proportion of patients receiving oral anticoagulation treatment. It was noted that PSM might also improve the TTR for patients with initially poor control.

In a subsequent trial to evaluate the clinical effectiveness of PSM with dosage adjustment compared to routine care outside of trial conditions, 38 patients from

the original Fitzmaurice *et al.* study[256] performing PSM were matched with 40 controls whose warfarin was managed in primary care.[257] In a 12-month period, the TTR was 70% for patients performing self-management and 57% for control patients, demonstrating again that PSM with dosage adjustment is effective when compared to usual care outside of trial conditions.

Most recently, Heneghan *et al*. performed a meta-analysis of 11 trials (encompassing 6,417 patients) comparing PSM to conventional care.[235] Rather than aggregating previously published information, they merged the individual patient data, allowing for time-to-event analyses, analyses of sub-groups and outcomes, and increased statistical power. The authors found that PSM improved INR control and TTR when compared to usual care. They also found that PSM resulted in a significantly reduced incidence of thromboembolic events, with a 49% risk reduction (HR 0.51, 95%CI 0.31-0.85, p=0.010). However, they found no significant difference in bleeding rates or mortality between the groups. This is contrary to the findings of their previous meta-analysis which showed improved mortality in those performing PSM.[200] The authors suggest this difference may have been contributed to by the results of one large included study and their inability to obtain data from 10 other identified and eligible studies.[235] Subgroup analyses showed the greatest reductions in TE events were seen in those self-monitoring and self-adjusting their doses. The authors also found that the largest reductions in TE events were seen in younger patients (<55 years if age) and those with mechanical heart valves. PSM did not significantly change rates of adverse events in the very elderly (≥85 years of age), and appeared to reduce mortality in this group.[235]

In summary, studies have shown PSM to be feasible, accurate, associated with a greater time in therapeutic range, and an improved quality of life for patients. International research has established that PSM represents the gold-standard for

warfarin management for suitable individuals,[200] and that patients who perform PSM have been shown to spend a greater proportion of their time within the target INR range, have a lower incidence of haemorrhagic and thromboembolic events and also potentially have a lower risk of mortality compared to patients undergoing usual care.[199] PSM has been noted as an effective method of monitoring oral anticoagulation therapy, providing outcomes at least as good as, and possibly better than, those achieved with anticoagulation clinics or usual care.[143, 200, 233]

PSM has also been shown to have a number of benefits for participating patients that extend beyond simply improving control of the INR. Patient empowerment is a concept which entails the redistribution of power between patients and physicians, with patients taking control of their own health and interactions with health professionals.[258] Patient empowerment can occur on a number of levels, from simply being given more information on the condition to having full control of medical decision making.[258] Empowering patients is one of the means by which PSM has been proposed to improve patient outcomes.

While it has been clearly demonstrated that PSM has an important role to play in improving the INR control of patients taking warfarin, PSM of warfarin therapy has also been demonstrated to improve thromboembolic and haemorrhagic outcomes, with only a slight increase in the percentage of INR tests in the therapeutic range.[259] In this study improvements in clinical outcomes were achieved without an improvement in INR control; thus, the benefits of PSM extend beyond improved INR control to increasing patient empowerment, improving adherence and improving patient awareness of their health status.[259]

Patients in a PSM study by Sidhu *et al.* reported greater personal convenience, increased confidence in their therapy, and enjoyed the ability to widely travel with less fear of deviation from the therapeutic range while away from home.[245] By

minimising hospital or primary care visits for blood sampling and providing close monitoring with an optimal higher test frequency and less discomfort for the patient, POC devices provide more flexible procedures for INR measurement and have also been shown to improve the quality of life.[200]

Ultimately, self-monitoring by patients with or without self-dosage adjustment, has a great potential to maximise the safety of anticoagulant therapy.[149] It empowers patients to assume responsibility for their own therapy, which can lead to improvements in patients' self-worth, closer adherence to treatment, and increased control of treatment with warfarin.[254, 260] It has been demonstrated that self-monitored patients are less anxious about their therapy.[149] Other advantages of PSM include patients having the ability to conduct testing at home, saving travel and time to visit a clinic or doctor, and that they are less dependent on the healthcare system to manage their therapy.

2.4.3.1.2 Requirements for performing self-monitoring

Despite the many advantages associated with this model of care, PSM may not be a unanimously appealing or appropriate option for all healthcare providers or patients. It is a model of management which requires special training to implement,[24] and there are still many variables, such as patient selection criteria and testing frequency, that need optimisation.[243]

2.4.3.1.2.1 *Patient-centred requirements*

A number of criteria relating to patient selection and potential capability to undertake PSM have been identified in a range of studies. These include a long term indication for warfarin,[253] being an adult or supervised by an adult,[249, 261] a willingness to learn the testing procedure and perform PSM,[243] and a basic understanding of, or capability to understand the condition for which warfarin is prescribed.[243, 253, 262, 263] Patients, or their carers, also require sufficient manual

dexterity and acuity of vision to operate the testing device.[143] A contraindication to participation in PSM is the presence of antiphospholipid antibodies, including lupus anticoagulant, as the test strips of commercially available POC devices are inaccurate in the presence of these antibodies.

It has been suggested that most patients who are able to lead an independent and self-supporting life are, in principle, capable of undertaking PSM, regardless of education and social status.[129, 143, 149, 235] However, it is widely accepted that PSM is not an appropriate management model for all patients taking warfarin. A Cochrane review examined a population of 11,738 patients from 14 trials.[233] The average proportion of patients who could not (or would not) take part in PSM was 68%, with a range of 31% to 88%. Of the patients assigned to the intervention, 24.9% (range 0% to 57.3%) were unable to complete self-monitoring.[233] The main reasons for drop-outs were problems with the monitoring device, physical limitations preventing PSM, problems with attending training, or failing the training assessment.[233] Trials have suggested that the proportion of patients eligible to undertake PSM may be as low as 16%[260] or as high as 80%.[264] Regardless of the actual proportion of patients who would be able to undertake PSM, it is important to recognise that PSM is not suitable for everyone. However, it is also important to remember that PSM represents a model of care with the potential for improvements in both clinical and patient-centred outcomes, and it is a model that should be more widely available to those who are willing and able to participate.

2.4.3.1.2.2 *Educational requirements*

Adequate patient education and training is also essential to the success of PSM. In all trials involving anticoagulation self-monitoring, patients have undertaken comprehensive training programs, and the training process has been identified as critical in achieving the benefits of PSM.[149, 190, 191, 240, 242, 245, 260, 265, 266] Most studies

have incorporated multiple training sessions, involving training on the use of the equipment and instructions on dosage adjustments, though some studies are not specific about their methods or requirements. Ansell et al. simply had their patients instructed on the use of the INR monitor and in dosage-adjustment guidelines by an anticoagulation nurse over a two-week period.[190] Other researchers have placed more importance on the training programs their patients undergo in order to self-monitor. Common elements appear in many of the suggested programs.[149, 191, 242, 245, 260, 265, 266] In most training programs, patients receive an overview of oral anticoagulant therapy, including the effect of certain factors, such as alcohol and diet, on anticoagulation control. Patients also receive information on the importance of bleeding and thromboembolic events, and how to recognise the signs of over- and under-coagulation. As well as theoretical information, it is suggested patients receive intensive supervised training on the use of POC monitors, and instruction in adjustment of warfarin dose (if required). Some programs give patients the opportunity to practice obtaining consistent INR results at home between training sessions.

In Germany, a nationally approved, formalised training program developed by Sawicki *et al.* is in place.[191] This structured educational program aims to help patients assume increased responsibility for disease management based on systematic INR self-monitoring and self-adjustment of the warfarin dose. The training course covers theoretical and pharmaceutical aspects of anticoagulation, a demonstration of the equipment to be used by the patients, and a practical session using POC testing systems.

Fitzmaurice *et al.* have also developed a training program for patients in UK studies of PSM.[267] Their training course involves two workshops of up to two hours, conducted a week apart. These workshops are conducted within general practice

settings and cover theoretical and practical aspects of anticoagulation management, including the procedure for performing testing, the use of testing devices, quality control procedures, and managing the INR result using a specified algorithm. Between sessions patients are asked to practice with the POC device, recording at least six results and any problems. The research team individually assesses each patient to determine whether they are competent to self-manage.

The role of education is particularly important for patients who will go on to assume a greater responsibility for managing their own therapy through PSM. Hence, the development of comprehensive, locally appropriate education and training packages to support the implementation of PSM is essential to ensure optimal outcomes from PSM can be achieved.

2.4.3.1.2.3 *Quality assurance requirements*

There has been much debate in the literature surrounding the quality assurance requirements for patients undertaking PSM. The accuracy of POC INR devices, such as the CoaguChek®XS device, in the hands of patients has been well established.[127, 192] However, pathology laboratories performing INR testing are required to undertake a process of quality assurance to ensure both internal and external quality control of the INR results measured.[65] This has ignited discussion over what quality control requirements are necessary for POC INR devices.

The CoaguChek®XS device has inbuilt internal quality control (IQC) within the test strips to ensure that test strips have not been damaged and that the machine is capable of producing a reliable result. Thus, IQC is performed every time an INR test is conducted.

External quality control (EQC) is more complex to achieve. Laboratories and anticoagulation clinics are encouraged to undertake accredited EQC programs, such as the National External Quality Assessment Scheme (NEQAS) in the UK,[268] or the

Royal College of Pathologists of Australasia Quality Assurance Program (RCPA QAP) in Australia.[269] In the UK, a NEQAS programme specifically for patient self-testing is now available,[65] making EQC by an externally accredited program achievable. However, in Australia the QAP program requires a number of reasonably complex steps to be undertaken to test a sample and the annual cost of enrolment makes it prohibitive for individual patients to enrol. The small number of patients performing self-monitoring in Australia means there is currently little demand for the expansion of the RCPA QAP program. As such, other options for EQC need to be explored.

There have been two alternative methods for EQC suggested in the literature. One option is for patients to take their monitor to a clinic that participates in an externally accredited EQC program and to compare the results obtained with their monitor to results obtained with a monitor enrolled in an external program.[65] A second option is to measure the INR simultaneously at a laboratory, via venous sample, and using the patient's POC monitor.[239] INR differences of up to 15% between the two samples would be considered acceptable for clinical purposes,[261] especially as such a difference may also be demonstrated between tests on the same sample in different laboratories due to differences in the collection and testing procedures at different sites.[261] It is recommended that this form of EQC be carried out every 6-12 months for stabilised patients performing PSM.[65] This method was successfully trialled with PSM patients by Tripodi *et al.* who concluded that such comprehensive EQC systems would make monitoring of oral anticoagulant treatment by PSM safer and more effective.[270]

The aim of introducing PSM is to improve the quality of anticoagulation therapy, including increasing the safety and efficacy of warfarin through improved INR

control. Hence, the inclusion of quality assurance procedures to guarantee accurate and reliable results is imperative to ensure this goal is achieved.

2.5 Patient perceptions of taking warfarin

Warfarin is a medication that has been widely used for more than half a century, yet very few studies have explored patients' perspective on taking warfarin. Of the small number of qualitative studies that have been done in this area, most focus primarily on barriers to warfarin use and preferences for treatment options.[271-273] Bajorek *et al.* conducted a series of interviews with health professionals, patients and carers to explore attitudes and identify ways to improve the management of warfarin in older patients.[271] They found that patients reported a lack of information provision and education on the role and importance of warfarin therapy. This impacted on their confidence in taking warfarin and was the foundation for the major recommendations of strategies to improve warfarin management made by the authors. Dantas *et al.* also conducted interviews with older patients to examine the experience and perspective of people on long-term warfarin.[272] Similarly, they found that patients reported insufficient education and information provision. During the interviews, patients also expressed a general satisfaction with their warfarin regimen, despite reporting that it impacted on their day-to-day lives. Aspects of treatment which were described as impacting on their lives included the need for regular dose adjustments, and the subsequent need for INR tests, the need to alter or monitor their diet and alcohol intake, and an increased sense of anxiety related to the risk of bleeding and drug interactions. The burden of warfarin has also been described by Wild *et al.*[273] Participants in their study were similarly concerned by bleeding and bruising, including the cosmetic embarrassment which may accompany bruising, the inconvenience of INR testing, travel, dietary

restrictions, drug interactions, and the time involved, particularly for employed participants.

A further study by Bajorek *et al.* involving patient focus groups again reiterated the experiences of patients receiving inadequate education and information.[161] They went on to discuss patients' reactions to being on warfarin and the spectrum of experiences with warfarin that were described. Patients progressed through a 'cycle of reactions' regarding warfarin, describing fear, followed by acceptance, and then forms of dependence. The patients had generally had few problems with warfarin and described satisfactory experiences overall. Interestingly, the paper also raised the topic of warfarin self-management. The term was used in this context to discuss the ways in which patients described managing their warfarin, not self-management in the sense of monitoring their INR and self-adjusting their dose as is used elsewhere in this thesis and the literature. Bajorek and colleagues also described participants being quite happy to hand over the management of concomitant medication to an external party but remaining very much in control of their warfarin:

> *Many attached a special significance to it, developing routines or systems that essentially provided them with a coping strategy for [managing their warfarin therapy]. What the routine entailed was not important, as each participant described their own individualised method, but rather that it was an intimately understood process that empowered them to confidently manage their warfarin.*[161]

While this is not self-management in the sense that is generally discussed in the literature, it is an important description of the significance patients place on maintaining an element of control over their warfarin treatment. This becomes especially important when looking at the perceptions of PSM of warfarin therapy.

2.5.1 Patient perceptions of self-monitoring

Self-monitoring is a term that is widely used in the literature and is probably best described by Wilde and Garvin, who suggested that the process of self-monitoring is composed of two complementary attributes: awareness of bodily symptoms, sensations, daily activities and cognitive processes; and measurements, recordings and observations that inform cognition or provide information for independent action or consultation with care providers.[274] Self-monitoring is a part of managing many chronic conditions and perhaps the most similar to the self-monitoring of warfarin therapy is blood glucose testing in diabetes. While the clinical benefits of self-monitoring in non-insulin dependent diabetes are contentious,[275] patients with both insulin-dependent and non-insulin dependent diabetes describe the advantages of self-monitoring as providing them with a sense of control, peace of mind, a sense of 'success' and an ability to actively manage their condition.[276, 277]

Much of the INR self-monitoring literature describes similar patient-centred benefits of this method of management. A number of studies have described patients expressing a strong preference for PSM compared to their usual model of care.[191, 192, 278] Other studies have reported improvements in quality of life and other measures of patient satisfaction resulting from PSM.[129, 243, 245, 259, 279, 280] Anderson *et al.* describes patients preferring PSM as they found the portable testing model to be more convenient and less painful than traditional laboratory monitoring.[192] Patients in this study also reported that the use of the portable monitor gave them a greater sense of involvement and control over their medical condition.[192] These results were echoed by Cromheecke *et al.* and Sawicki who described an independence from usual care improving both self-efficacy and patient satisfaction with anticoagulation treatment.[191, 278] Other reasons proposed for the observed improvements in patient satisfaction and quality of life include an independence

from usual care,[200, 279] increased personal convenience, including the ability to travel and better organise free time,[200, 245, 279, 280] and increased confidence in anticoagulant therapy.[245] These studies were primariliy of quantitative design and patient feedback was assessed through questionnaires. They were able to provide no greater detail on aspects such as why patients preferred PSM over usual care or why they found laboratory testing inconvenient.

One qualitative study exploring patient perspectives of PSM was identified.[281] This study qualitatively analysed the content of 246 blog posts made on the internet by 108 individual patients or carers over a 10 year period. Most of the bloggers were from the USA or the UK. They identified similar patient-centred benefits to the studies described above. They reported key themes relating to patient benefits, equipment, and social issues. Patient benefits included PSM saving patients' time, providing a level of personal control, increasing patient choice, reducing the travel and costs associated with convential INR testing, and providing peace of mind. Social issues included the pain and stress of taking warfarin and of INR testing. Despite there being advantages to using blogs for qualitative research, including the readily available and accessible information and the anonymity of participants, there are also disadvantages to this form of data.[282] Disadvantages include an inability to identify bloggers' demographic details and to delve for deeper information on topics raised.[283] These disadvantages prevented the researchers probing more deeply to understand the reasons behind some of the views expressed in these forums. It is also likely that the views included in analyses of blog posts are those of technologically savvy patients who feel comfortable expressing their views in a public forum. Many people taking warfarin are older and, in many instances, less likely to be ready to embrace online technologies.

2.6 Evolution of pharmacist-delivered services

The focus of pharmacy as a profession has evolved dramatically over the last century. Pharmacy entered the twentieth century in the role of apothecary, primarily focussed on compounding and dispensing medicinal products.[284] Pharmacists were sought out by physicians for advice on the most practical means of providing medication for their patients and enjoyed high levels of job satisfaction.[284]

By World War II the role of preparing pharmaceuticals was being taken over by the growing pharmaceutical industry and the choice of drug was increasingly transferred to the physician. This change left pharmacists focussed on dispensing manufactured medicinal products, sometimes referred to as the 'count and pour' period.[284] The highly developed technical skills of pharmacists were no longer needed in everyday practice and pharmacists became lost professionally.[284] As Mrtek and Catizone put it:

> *The loss of such deeply rooted functions endangered the identity of the entire profession … the changes in practice had left a limited role for community pharmacists, the simple dispensing of drugs on order of the prescriber, with its associated monetary transaction. Everything else had been swept aside by progress.*[285]

Pharmacists were searching for their place as health professionals, over and above simply being dispensers of prescriptions and over the counter medications.[284]

Clinical pharmacy emerged in the mid-1960s and pharmacists began to perform functions new to the practice of pharmacy and to seek fulfilment of their professional potential.[286] Brodie introduced the concept of drug-use control, which linked the professional responsibility of the pharmacist to patient welfare and

required a patient-pharmacist relationship to be formed.[287] He also introduced the term 'pharmaceutical care' which he defined as:

> *The determination of the drug needs for a given individual and the provision not only of the drug required but also the necessary services (before, during and after treatment) to assure optimally safe and effective therapy. [Pharmaceutical Care] includes a feedback mechanism as a means of facilitating continuity of care by those who provide it.*[288]

Brodie recognised the need for pharmacy to grow beyond a profession with a purely distributive function, to one where pharmacists apply their scientific knowledge to benefit public health and safety.[289]

In 1990 Hepler and Strand also discussed a concept of pharmaceutical care which they defined as "the responsible provision of drug therapy for the purpose of achieving definite outcomes that improve a patient's quality of life."[286] Their definition shares a basis with the work of Brodie in that it involves pharmacists taking responsibility for the therapeutic goals of drug therapy being achieved and ensuring that drug-induced illness does not occur.[286] Their concept was based on a similar premise of professional responsibility for patient welfare[286] and on the words of Cipolle: 'drugs do not have doses, patients have doses.'[290]

Despite the identification of the pharmaceutical care concept by Hepler and Strand over 20 years ago, the pharmacy landscape remains, in many ways, largely unchanged. The transitional period for pharmacists regaining a clear professional identity continues. Twenty years ago pharmacy was described as "a profession in search of a role".[291] While this new role is developing, the new focus of pharmacy as a profession is yet to be fully elucidated.

The emerging role for pharmacists looks set to incorporate elements of both drug distribution and service provision, encompassing the patient-orientated responsibilities of pharmaceutical care as defined by both Brodie and Hepler and Strand. Pharmaceutical care is being translated to patient-orientated practice through cognitive pharmaceutical services.[292] These can be defined as "professional services provided by pharmacists, who use their skills and knowledge to take an active role in patient health, through effective interaction with both patients and other health professionals."[293] The successful integration of cognitive pharmaceutical services into everyday pharmacy practice may not only improve the outcomes of patients but also the professional satisfaction and identity of pharmacists.

Steps have been made in Australia to forge new roles for pharmacists in pharmaceutical care roles. In 1990 the Pharmacy Guild of Australia and the Commonwealth Government entered into the first of a series of Community Pharmacy Agreements (CPAs) which set out the remuneration that pharmacists would receive for dispensing Pharmaceutical Benefits Scheme (PBS) medications and the location rules governing pharmacies approved to supply PBS medications.[294] Over time these Agreements have evolved and increased their scope to provide for the provision of certain professional programs and services.[294] Specific funding for professional pharmacy services was first provided under the second Agreement, with $5 million being allocated.[295] By the fourth Agreement this figure had increased to $568 million, for services covering the provision of dose administration aids, diabetes management and medication reviews.[295] The fifth CPA, which commenced in July 2011, saw an increase in the pool of funds available for professional programs and services to $663 million.[295]

One important program which has been implemented as part of the CPAs is the Home Medicines Review (HMR) program. This program is designed to assist individuals living at home to maximise the benefits of their medicine regimen and prevent medication related problems.[296] The objectives of the HMR program are to:

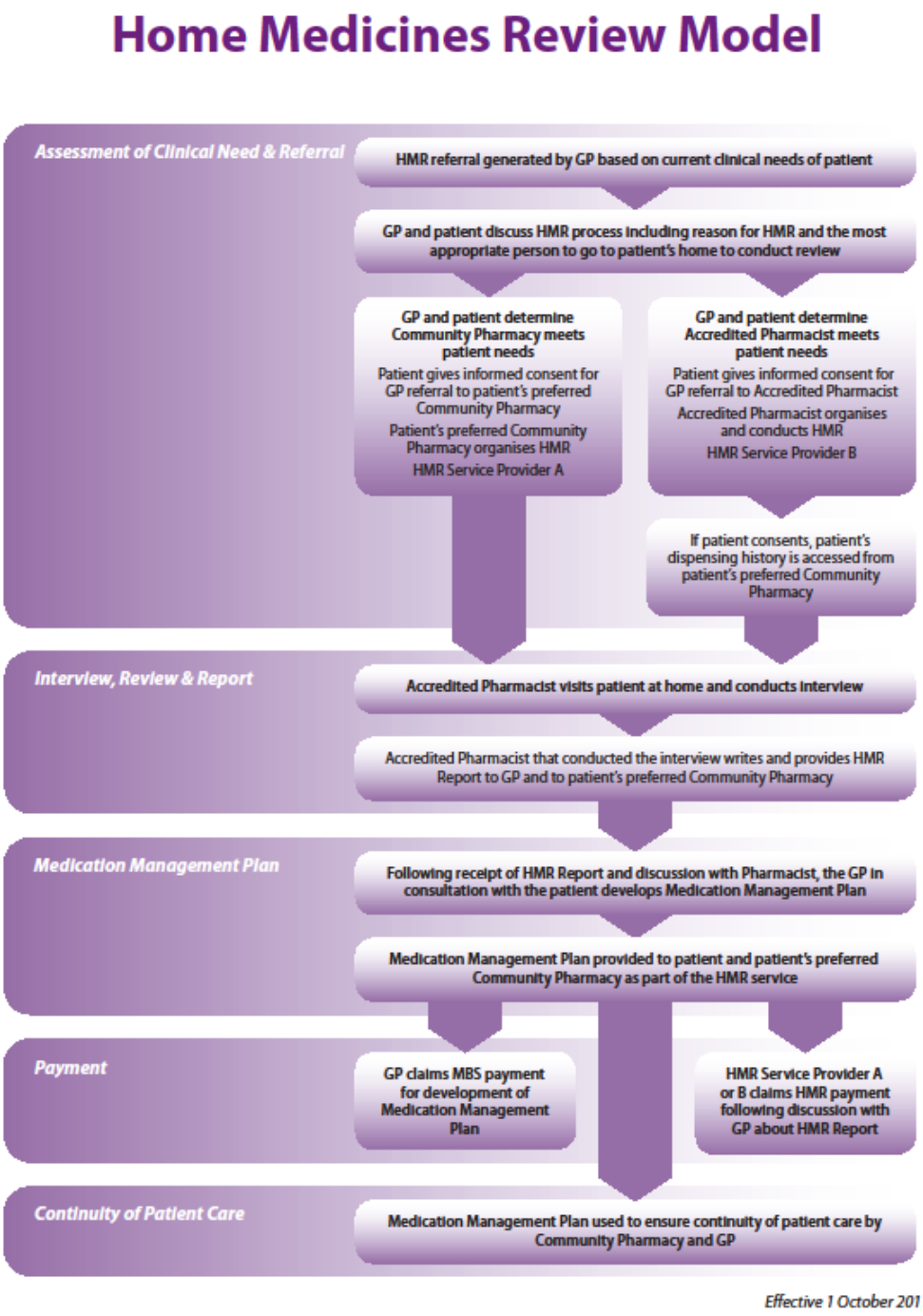
- achieve safe, effective, and appropriate use of medicines by detecting and addressing medicine-related problems that interfere with desired patient outcomes;
- improve the patient's quality of life and health outcomes using a best practice approach, that involves cooperation between the GP, pharmacist, other relevant health professionals and the patient (and where appropriate, their carer);
- improve the patient's, and health professional's knowledge and understanding about medicines;
- facilitate cooperative working relationships between members of the health care team in the interests of patient health and wellbeing; and
- provide medication information to the patient and other health care providers involved in the patient's care.[297]

The HMR process essentially involves a patient, after referral by their GP, being visited at home by an 'accredited' pharmacist who reviews their medication regimen, delivers education and provides the GP with a report and medication suggestions. The GP then agrees on a medication management plan. An 'accredited' pharmacist is "an experienced pharmacist who has undertaken specified education programs or examinations, approved by the Australian Association of Consultant Pharmacy or the Society of Hospital Pharmacists of Australia", as well as completing continuing specified professional education and regular reaccreditation.[296]

The referral process originally required GPs to refer their patient to the community pharmacy of the patients' choice to facilitate an HMR with an accredited pharmacist. Changes were made in the fifth CPA which came into effect on 1 October 2011 that enable a GP to refer directly to an accredited pharmacist of choice (Figure 8). Further changes are proposed under the fifth CPA to enable referrals to be made by hospital physicians to facilitate timely HMR provision following discharge from hospital.

The HMR program was the first Australian example of a remuneration model for pharmacists that is not linked to the dispensing and provision of medicines. It is also the first service that has been funded under the CPAs that is provided in the community, not within the confines of the pharmacy. It is an important step in the evolution of the role of pharmacists towards one focussed primarily on the provision of cognitive pharmaceutical services to improve patient outcomes.

Figure 8: HMR pathway as at October 2011[296]



2.6.1 Implementing pharmacist-delivered services

Implementing cognitive pharmaceutical services within the practice of pharmacy requires a process of change to occur, both in pharmacy practice environments and in the attitudes of those who will be delivering the services. Community pharmacies within Australia form a broad network of potential service providers spread across the country, though they generally remain quite separate and essentially function independently from one another. Williamson commented on the difficulty of achieving change across a fragmented network of organisations, such as community pharmacies, noting that change can often be hindered "not because people are necessarily opposed to the changes, but because there are not the structures or mechanisms which can bring them together in an appropriate manner to make [the changes] happen".[298] Recent pharmacy literature within Australia has discussed the need for a change management strategy to support such structures to enable the evolution of community pharmacy practice to a service delivery orientated model and to overcome barriers to service provision.[295, 299]

Barriers to service provision and the widespread introduction of pharmaceutical care were identified from the outset of the period of change; barriers both within and external to the pharmacy profession.[291] The move from a pure focus on product distribution to one where the pharmacist would influence decisions regarding the use of the drug and share in the accountability of effects was identified as a barrier likely to face product-orientated practitioners.[291] Similarly, pharmacists solely focussed on the provision of a service without regard for the outcomes of therapy were also seen to be a challenge to the introduction of a pharmaceutical care model.[291] External to the profession, one of the major barriers identified was the method by which pharmacists are compensated.[291] The impact of traditional fee-for-service models, such as the remuneration model for dispensing, was seen as a

serious impediment to the provision of comprehensive pharmaceutical care services.[291] Despite discussions of pharmaceutical care being a cooperative activity with other health professionals,[286] potential attempts by other healthcare groups to keep pharmacists in their traditional role and out of the healthcare team were also identified.[291]

Pharmacists themselves have cited barriers such as a lack of confidence in their own clinical skills, a lack of time to implement pharmaceutical care services, costs involved in providing higher levels of services and a lack of corresponding remuneration, the physical layout of the pharmacy, concerns about negative changes in the pharmacist-patient relationship and disapproval from medical practitioners.[300, 301] Providing new pharmacist-delivered services also often requires the development of new skills, such as making physical assessments, educating patients, administering patient outcome measures, and documenting pharmacist-patient encounters,[302] which in turn require time and potentially training to develop.

However, not all pharmacists are resistant to change and many practitioners see the move to service provision as a way to ensure the future viability of the profession[303] or as a way to improve their personal level of professional satisfaction.[304] One study identified four dominant attributes possessed by innovative pharmacy practitioners delivering advanced pharmaceutical services.[304] They were a philosophy of practice, a patient care process, a management system, and clinical knowledge.[304] They went on to develop a checklist of essential components for developing an innovative community pharmacy practice covering aspects of these four attributes. Their diverse checklist agreed with the work of others, including Farris, who stated that pharmaceutical care implementation programs which address individual factors singly and in isolation will not be successful.[305]

While it is important to be aware of the barriers facing the implementation of pharmacist-delivered services, perhaps it is more important to consider the facilitators of practice change. An Australian study focussed on identifying the facilitators of practice change relating to the implementation of community pharmacist-delivered services.[306] They identified the following facilitators to service implementation:

- Remuneration of implementation and/or service;
- External support or assistance;
- Reorganisation of the pharmacy's structure and function;
- Communication;
- Internal leadership; and
- Delegation of tasks.

They also identified motivators of practice change, such as a desire for professional satisfaction, a desire to provide healthcare to the public, and a fear of threats to the pharmacy business.[306] Perhaps not surprisingly they found that the success of a practice change attempt is strongly linked to the philosophical values of the pharmacists involved.[306]

2.6.2 Pharmacist-delivered services

Fuelled by the need for the pharmacy profession to shift its focus, and implement pharmacist-delivered services, studies have been conducted to provide evidence on how pharmacists can improve patients' outcomes.[307] A wide range of chronic disease states have been targeted, including diabetes,[308-313] respiratory conditions such as asthma and chronic obstructive pulmonary disease,[314-317] cardiovascular

diseases including hypertension and dyslipidaemias,[318-322] chronic pain,[323] smoking cessation,[324, 325] and opioid dependence.[326]

Despite the range of different disease states being targeted, the pharmacist-delivered services described share many common elements. The Asheville Project of North Carolina represents perhaps the largest ongoing set of studies of pharmacist-delivered services to date and is a model of care that has been adopted in many other American states. The Project was originally commenced to examine the clinical, economic and humanistic outcomes of pharmaceutical care services provided for patients with diabetes.[308-311] It was later expanded to also encompass pharmaceutical care services for asthma and patients at high cardiovascular risk.[327, 328] Pharmacists involved in providing services under the Asheville Project undergo training in the disease state relating to the service they intend to provide and conduct patient visits as per the protocol for that condition. The protocol for patient visits involves an intensive face to face service which includes counselling and self-care education, the setting of goals for self-care/self-monitoring of the condition, relevant testing or review of patient-obtained test results (such as blood sugar readings, blood pressure readings, or peak flow measurements), relevant assessments or examinations (such as inhaler technique, medication-related problems, or eye and foot examinations), and referral to other healthcare professionals where appropriate.[308-311, 327, 328] The ImPACT project also addressed the role of pharmaceutical services in cardiovascular disease, focussing on hyperlipidaemia, and similarly encompassed pharmacist-delivered POC cholesterol testing, medication related factors, and the setting of patient goals.[318, 319]

In Australia, recent studies have examined the use of an Asheville-type model of pharmacist-delivered services in Australia for patients with diabetes, asthma and cardiovascular diseases.[312-316, 322] These studies again saw pharmacists involved in

the provision of the service being intensively trained in the disease state and the issues surrounding optimal management and outcomes for patients with this condition. They were then guided by a protocol which covered the elements of the pharmaceutical care service. The services all involved face to face visits where pharmacists performed relevant monitoring of the condition and undertook behavioural change strategies to encourage goal setting and patient self-management and monitoring of their condition. Subsequent visits aimed to reinforce these goals and provide ongoing support to facilitate their achievement. Medication assessments were undertaken, along with relevant patient education and counselling and referral where warranted.

Consistent throughout all the studies described above is the use of a private counselling area where education and relevant testing and assessments can be conducted. Also common to all services described was a significant investment of time on the part of the participating pharmacist. This time commitment not only relates to the training necessary to up skill to be proficient in the provision of the service, but the time required for provision of the service in the pharmacy setting. The face to face consultations took an average of 30 minutes per patient per visit and visits were as frequently as monthly for each patient.[327, 328] Hence, there are factors external to the motivation of pharmacists which are likely to impact the success of service implementation outside of trial conditions. Pharmacists in Australia are potentially less likely to perceive the initial training as a significant time burden in light of current changes in registration requirements, as this training can be used to contribute towards recently introduced mandatory continuing professional education requirements of pharmacist registration. However, the perceived burden of the time required to provide the service is likely to depend heavily on the workload pressure in the pharmacy in which they work, including the availability of additional pharmacists to assist with the everyday duties. The

services provided as part of the Asheville Project are funded through insurance companies, enabling pharmacies to ensure that an adequate number of pharmacists are employed to provide a successful service. This funding ensures the sustainability of this model of professional service delivery. Unfortunately, professional services such as those described above are not currently remunerated under the Australian healthcare model, a factor which is likely to impact on the success of any attempts to implement similar service models in this country.

2.6.3 Pharmacist-delivered anticoagulation services

As described above, community pharmacists are in a unique position to help patients manage chronic illness in view of their expertise, their regular contact with patients and their accessibility. The management of chronic anticoagulation therapy is yet another area which lends itself to pharmacist-delivered services, and internationally pharmacist involvement in warfarin management has been shown to result in significantly better control of the INR.[329-331]

Pharmacists may be involved in warfarin management in a number of settings, but most studies describe the role of pharmacists in inpatient anticoagulation care,[208] and in anticoagulation clinics, both outpatient clinics situated within hospitals[329, 332] and in the community setting.[331] Community pharmacists in the USA have been shown to be able to successfully manage anticoagulation therapy while operating under collaborative practice agreements; using POC INR devices to obtain results, making dose adjustments where needed, and providing ongoing patient education and support.[333] Similar benefits of pharmacist-delivered anticoagulation services have been reported in studies from Canada,[208, 331, 334] Australia,[335, 336] and New Zealand.[337]

As with the pharmacist-delivered chronic disease services discussed previously, the anticoagulation services described all require the pharmacist to have undergone an

initial period of training. The services themselves then comprise elements of POC testing, patient education, discussing the target INR control aimed for and ways to achieve this, medication and compliance assessments, and referral to other healthcare providers where indicated. High levels of patient satisfaction have been reported by users of pharmacist-delivered anticoagulation services.[333, 335]

Pharmacist-run anticoagulation clinics have been shown to impart a number of benefits. They improve the measures of INR control and reduce anticoagulation-related adverse events, through reducing both rates of major bleeding and thromboembolic events.[205, 214] They also have economic benefits, reducing the costs associated with warfarin management through reducing warfarin-related hospitalisations and emergency department presentations.[214] Such clinics have been operating in a range of countries for many years, but have traditionally involved the use of laboratory INR testing, reducing the convenience associated with a clinic-based system, as samples need to be drawn an hour before the scheduled consultation or the dosage advice and follow-up needs to be provided over the telephone.[329, 332, 338]

Point of care INR devices have enabled a change in the operation of pharmacist-run anticoagulation clinics.[209, 333, 335, 336, 339, 340] Pharmacists using POC technology have the ability to obtain the INR results during the scheduled consultation, enabling dosage adjustments to be communicated to the patient face to face and minimising risks of miscommunication. The use of POC devices also has the potential to increase the convenience associated with attending a pharmacist-run clinic, through reducing time costs associated with clinic attendance.[218]

While many pharmacist-run outpatient anticoagulation clinics based in tertiary care hospitals exist, the accessibility of pharmacists in the community and the emergence of pharmacist-run clinics in such settings have the potential to further improve

convenience, again through reducing the time and travel costs incurred by patients.[218] Community-based pharmacist-run clinics utilising POC technologies have the potential to form the basis of usual care management of patients on warfarin, increasing the accessibility of INR testing in both rural and metropolitan areas.

Most recently, a pilot study was conducted in a small rural town in New Zealand to assess the feasibility and potential benefits of managing warfarin through a pharmacist using POC testing and online computer decision support.[337] The initial pilot was conducted in a single pharmacy and showed significant improvements in the TTR during the study compared to the preceding period, with an improvement from 55% to 76%.[337] The service was conducted in collaboration with local doctors, who reported the service saving them time and improving their patients' understanding of warfarin. The pharmacist-delivered service was appreciated by patients, who all wanted to continue with pharmacist monitoring due largely to the finger prick blood testing procedure and the easy access to the pharmacy site.[337] This pilot resulted in a larger project being funded through the New Zealand government to assess the feasibility of introducing pharmacist-run anticoagulation clinics into community pharmacies across the country.

A previous study in rural areas of Australia also supported the notion of introducing community pharmacist-conducted INR monitoring.[335] Sixteen pharmacists received training on the use of the POC INR device and some basic educational materials relating to warfarin. Pharmacists then went on to receive referrals from local GPs and monitored the INRs of patients for approximately three months. The study found that the model of INR monitoring was well received by patients, pharmacists and GPs, and recommended that similar innovative service delivery models are needed to meet the requirements of rural Australians requiring warfarin.[336]

There are a number of facilitators and common elements to successful pharmacist-delivered services. One facilitator that needs addressing to implement innovative anticoagulation service delivery models in rural or metropolitan communities pharmacies is the provision of external support or assistance.[306] This assistance may be offered through the provision of resources to enable the implementation of a service. A common element of the pharmacy-based service delivery models discussed above was a comprehensive protocol covering all elements of the pharmaceutical service to be delivered.[308-310, 312, 313, 322, 327, 328] A service-delivery protocol, encompassing all aspects of the provision of an anticoagulation service, needs to be developed to facilitate and support the implementation of innovative pharmacist-delivered anticoagulation services within Australia.

PART TWO: THE ROLE FOR PHARMACISTS IN MANAGING WARFARIN

An exploration of pharmacist-delivered models of care

As previously discussed, the therapeutic benefits of warfarin are highly dependent on maintaining the INR within the target range.[341] Poor compliance, variable dietary intake, inadequate knowledge, and miscommunication between the patient and physician have all been cited in the literature as potential causes for fluctuations in the INR.[20, 62, 135, 141] A number of strategies have been suggested for reducing the risk of adverse events and improving INR control in patients taking warfarin. These include improving patient education, resulting in improvements in knowledge and compliance, adopting anticoagulation clinics in place of 'usual care', including the use of dosing algorithms or computer-assisted dosage adjustment in such clinics, and introducing patient self-monitoring (PSM) for suitable patients.[12, 137, 146, 148, 232, 241]

Models of care differ significantly between setting and countries, with advantages and disadvantages being evident for each different model (Table 4). The wide range of models of care has increased awareness of the various elements of each method of management that may be advantageous in other settings.

Table 4: Advantages and disadvantages of common models of care

	Advantages	**Disadvantages**
Physician managed care	Continuity of care Ease of access Reduced waiting times Familiar with all aspects of the patient's care Quality assurance in place if venous sampling used	Generally uses venous sampling Delay between venous sampling and dose adjustment Staff are not experts in anticoagulation Generally do not use computer-assisted dosage support
Anticoagulation clinic care	Use computer-assisted dosage support Expert staff dedicated to anticoagulation Dosage advice given during clinic visit High levels of quality assurance	May be a lack of continuity of care Generally involve long wait times Travel issues to central/hospital sites Generally uses venous sampling
Patient self-testing	Utilises point-of-care testing rather than venous sampling Convenient – no wait times or travelling Patient may adjust own dose and becomes the expert Patient empowerment	Expensive to patient (under current Australian healthcare system structure) Not all physicians are supportive Not suitable for all patients Quality assurance not embedded in practice Education and training not embedded in model

Optimising warfarin management

The literature suggests that there are a number of roles which pharmacists can play in the management of warfarin therapy in the community. Improving access to reliable warfarin education, timely INR monitoring, and facilitating PSM stand out as opportunities for pharmacists in Australia to pursue. To explore the potential feasibility of pharmacists fulfilling these roles, a number of complementary projects were designed and undertaken (Figure 9). This Part aims to explore areas that may be improved upon though enhancing the role of pharmacists to optimise the management of warfarin therapy in the community.

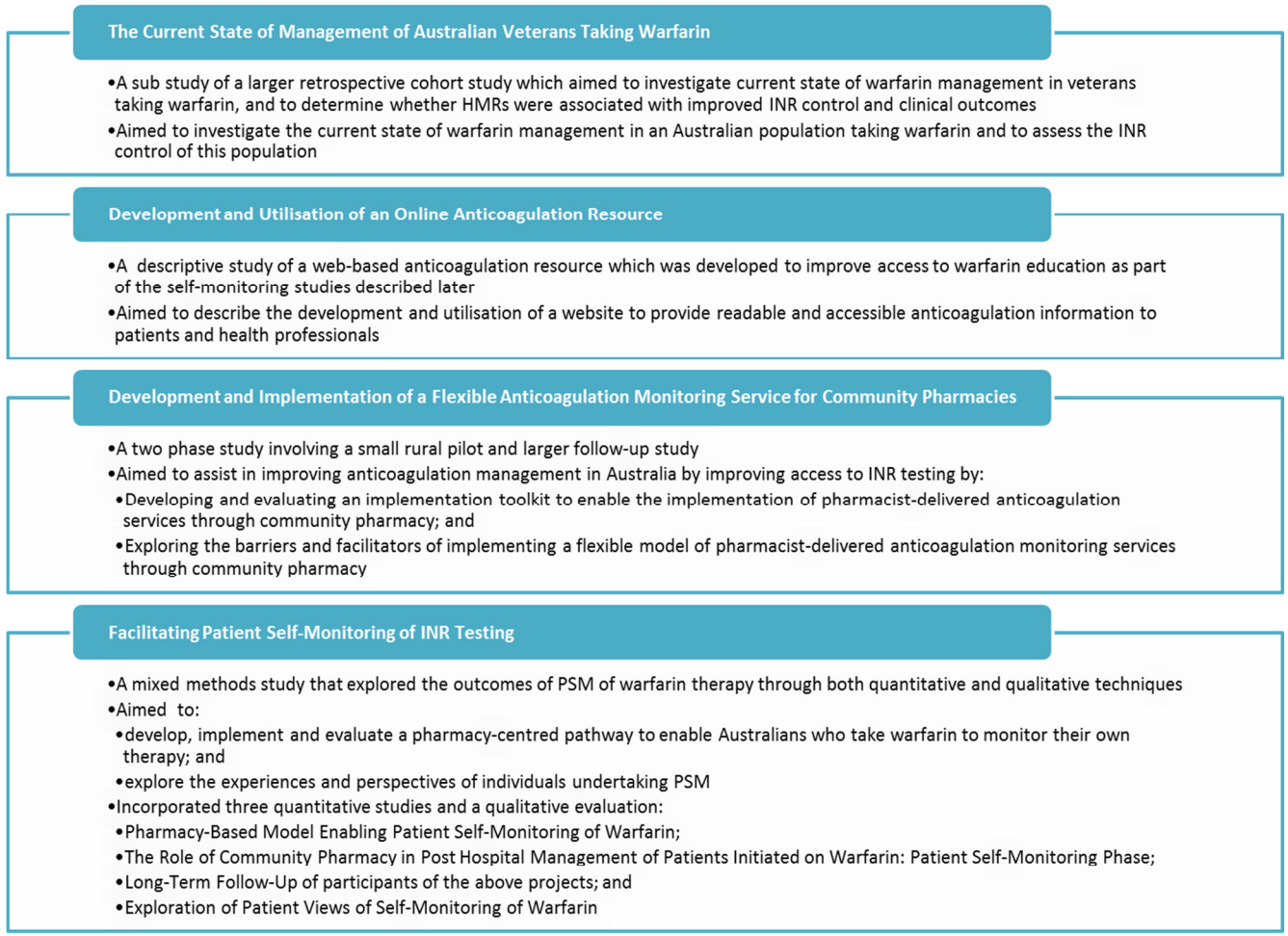
The INR control of a group of veterans was investigated to provide an idea of the baseline INR control in a cohort of community dwelling elders in Australia. A web-based resource was designed and promoted to improve access to reliable information on anticoagulant therapy. The website underwent a number of iterations to improve usability and design, and evolved to include functionalities to enable online recording of patient INR results.

The feasibility of pharmacists playing a role in improving access to INR testing was assessed through the development and evaluation of tools and resources to enable the implementation of pharmacist-delivered anticoagulation services, such as pharmacy-based anticoagulation clinics. This also enabled an exploration of what barriers and facilitators may impact on the success of such services.

The facilitation of PSM by pharmacists was explored from both a quantitative and qualitative perspective. A pathway utilising the existing HMR model was developed and evaluated, and the outcomes of PSM for patients were measured both in terms of potential clinical improvements and in terms of any changes in patient experiences.

Together these projects aim to provide a clearer picture of the role pharmacists practicing in the community may play in improving the quality use of warfarin therapy.

Figure 9: Description of studies which comprise the basis of the thesis



Stakeholder consultation

It was felt that it was important to consult a wide range of stakeholders in the design of the PSM pathway and on the development of materials used in the projects to ensure a model and resources which were seen as acceptable and feasible to participants at every step of the process. To this end, a Project Advisory Group was formed by inviting a wide range of stakeholder organisations to put forward a representative to participate in project discussions. The function of the Project Advisory Group was to inform and guide the research team to ensure optimal implementation of the projects.

The Project Advisory Group's role was to:

- provide advice regarding the feasibility of the implementation strategy of PSM in Australia;
- oversee and monitor the progress of the projects against the project plans and timelines and provide those directly involved on the project with guidance on project issues;
- identify and reduce barriers and risk to project implementation ensuring reconciliation of differences in opinion and approach, if disputes arose; and
- ensure that the requirements and perspectives of the participants were considered and that ethical guidelines were followed.

Individual reference group members were asked to act as 'knowledge brokers' within their organisation to assist the implementation of the projects.

Consumers, other healthcare professionals and industry were represented on the Project Advisory Group through input from:

- The National Stroke Foundation;
- The National Prescribing Service;
- The Royal Australian College of General Practitioners;
- The Australian General Practice Network;
- The Australian Medical Association;
- The Australian Association of Consultant Pharmacy;
- The Pharmaceutical Society of Australia;
- The Pharmacy Guild of Australia;
- The Society of Hospital Pharmacists of Australia; and
- The Royal College of Pathologists of Australasia.

Colleagues from the Universities of Sydney, Wollongong, and South Australia were also consulted and formed part of the post-hospital study project team. The services of a group of haematologists were engaged to enable the development of the PSM pathway and accurate and usable project tools.

Chapter 3 : The Current State of Management of Australian Veterans Taking Warfarin

3.1 Purpose of the study

The data arising from the PoCT represents that of a large population of Australians taking warfarin. However, it could be argued that their management in an unblinded study may not be reflective of the INR control of a wider range of Australians taking warfarin managed outside of study conditions. Overall, there is a lack of published data pertaining to INR control in an Australian setting.

Hence, this project aimed to retrospectively investigate the current state of warfarin management in an Australian population taking warfarin and to assess the INR control of this population. The Australian veteran population was chosen for the study as they are an elderly population, who are generally similar to the elderly Australian population. They are an especially useful population to study as the DVA funds most aspects of healthcare for many of its veterans, maintaining a unique linked database, meaning comprehensive data are generally available for the healthcare usage of veterans.

3.1.1 Context

The study that is described here was performed by Andrew Stafford, Luke Bereznicki and the author as part of a larger study aimed at assessing the impact of home medication reviews on the warfarin management of Australian veterans.

Medication reviews were first introduced in Australia in the veteran population by the DVA in 1999; a service later expanded to be the HMR program available to all Australians that we know today. A recent study by Roughead *et al.*[342] assessed the effect of HMRs in Australian veterans and war widows taking warfarin retrospectively using administrative claims data, however was unable to relate the

effects of HMRs to changes in INR results. This project was designed to investigate the INR control of a group of veterans taking warfarin, and to determine whether HMRs were associated with improved INR control and clinical outcomes.

The author was involved in the design of the larger study and the grant application process from the outset. Andrew Stafford's PhD research focussed on the cost-effectiveness of HMRs in Australia and the author had an interest in exploring the INR control of an Australian population. The home medicines review analyses were performed by Andrew Stafford and form part of his PhD Thesis. Andrew Stafford and the author performed the data extraction of INR control data. The author performed the analysis of the INR control data presented in this chapter.

3.2 Methods

3.2.1 Participants

The Australian Department of Veteran's Affairs (DVA) treatment population is comprised mainly of Australian defence force veterans and their eligible dependants, including spouses, widows or widowers, and children. For the purpose of this study, all people eligible for treatment under a gold card, including dependents, spouses, widows, widowers, and children, will be referred to as 'veterans'.

Over two thirds of the DVA treatment population have served in the Australian defence force, with 94% of those who served being male.[343] Reflecting this, in 2010 58% of the overall DVA treatment population were male and 70% were aged 70 years or over, with a mean age of 76.4 years.[343] This makes them a similar population to the general population of Australians taking warfarin. The PoCT suggested that 57.5% of Australians taking warfarin are male, with a median age of 73 years.[344]

The demographic spread of veterans by state and territory is shown in Table 5. Eligible veterans who hold a DVA gold card receive all health services and medicines funded under DVA arrangements.[345] White card holders receive health services and medicines for the treatment of specific conditions only under DVA arrangements.[345] The DVA treatment population comprises around 260,000 veterans, 208,000 of whom hold gold cards.[343]

Table 5: Distribution of DVA treatment population by state and territory (as at June 2010)[343]*

State or territory	n (%)
NSW	82,250 (31.9)
SA	20,427 (7.9)
ACT	5,404 (2.1)
QLD	62,239 (24.1)
TAS	8,155 (3.2)
VIC	54,991 (21.4)
WA	22,696 (8.8)
NT	1,150 (0.4)
Overall	257,312 (99.9)

* Note: 254 (0.1%) of Australian veterans reside overseas

3.2.2 The DVA database

The DVA claims databases contain details of all prescription medicines, medical and allied health services and hospitalisations provided to veterans for which DVA pay a subsidy. The DVA also maintain a client file, which includes data on gender, date of birth and date of death. The pharmaceutical claims database contains data on dispensed pharmaceutical items including: a unique DVA identifier, entitlement at time each item was dispensed, sex, date of birth, and pharmaceutical item details (PBS item code, name and strength, Anatomical Therapeutic Chemical (ATC) Classification System code,[346] date of supply, packs supplied and number of repeats). Hospitalisations are coded according to the World Health Organisation (WHO) international classification of diseases.[347]

3.2.3 Study design and data collection

This project is a sub study of a larger project which aimed to investigate current state of warfarin management in veterans taking warfarin, and to determine whether HMRs were associated with improved INR control and clinical outcomes.

The primary objectives of the larger study were to examine the influence of HMRs on the rate of serious adverse events leading to hospitalisation, and assess the INR control of veterans taking warfarin and whether this was improved by HMRs. It was hypothesised that veterans who received HMRs would have a reduction in hospitalisations due to adverse effects from their warfarin therapy and improved INR control compared to veterans who had not received an HMR.

A retrospective cohort study was undertaken to compare the outcomes of warfarin therapy in veterans who were exposed and not exposed to HMRs. The process undertaken by the research team to obtain consent from eligible veterans to be involved in the study, and subsequently receive data from the DVA and pathology laboratories is shown in (Figure 10).

As part of this larger study, eligible veterans were initially identified and selected by the DVA based on data from their patient database. To be eligible for inclusion in this study, veterans were screened by the DVA to meet the following criteria:

- Possess a gold repatriation benefit card;
- Be dispensed warfarin during the study period; and
- Be residing at home.

Criteria for exclusion were:

- Not taking warfarin; and/or
- Residing in a residential aged care facility (i.e. ineligible for a HMR).

The study period was 1 January 2007 to 31 December 2009. The DVA identified a list of veterans who met the inclusion criteria and who had also had an Home Medicines Review (HMR) prior to 30 June 2009. The DVA then randomly selected a

matching number of veterans who met the inclusion criteria who had not been exposed to an HMR in the study period. The HMR data enabled an analysis to examine the influence of HMRs on the rate of adverse events and INR control, which forms a part of Andrew Stafford's PhD thesis.

The identified veterans were sent an information sheet and consent form by DVA (Appendix 1). Signed consent forms were returned to the research team using the reply-paid envelope provided. A list of the veterans who provided consent was provided to the DVA.

The DVA retrospectively extracted data on all claims for eligible consenting veterans in the study period for the following health services: general practice consultations, specialist consultations, pathology services, and hospital admissions. In addition, they extracted counts of the number of prescriptions and unique medicines (defined by ATC code) dispensed and the demographic details of the veteran (including age, sex, remoteness of residence and number of comorbidities).

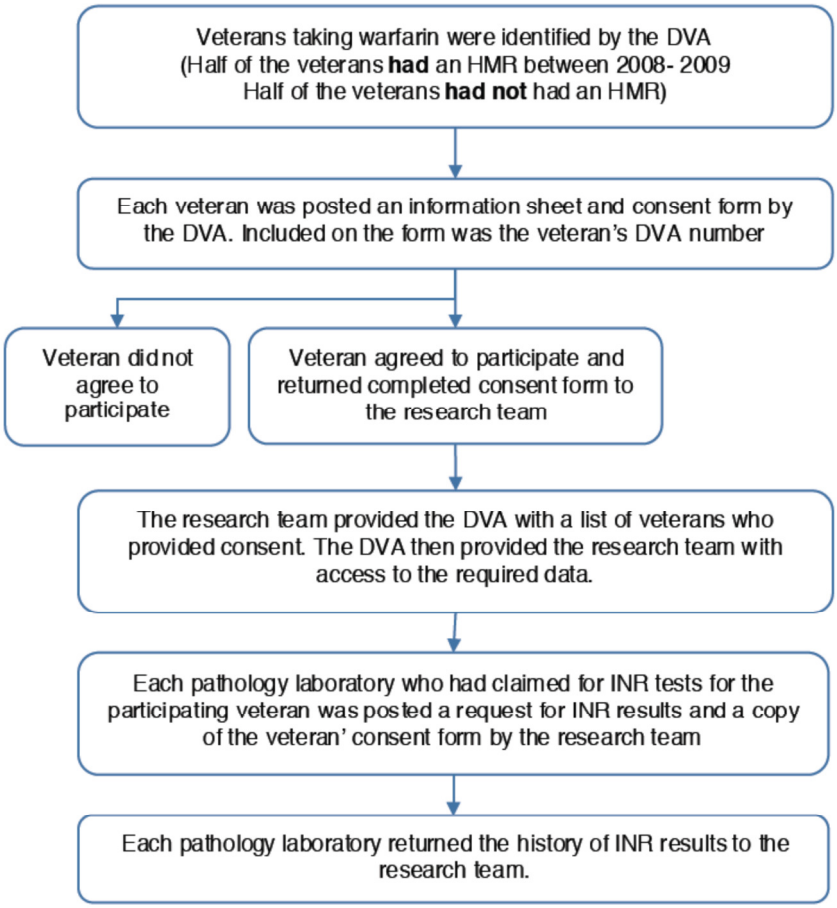
Following receipt of the data for consented veterans, secondary exclusion criteria were applied. Secondary exclusion criteria were:

- Consent forms received following the closing date for inclusion in the study;
- The veteran was deceased;
- There was no record of warfarin being dispensed; and
- The veteran had ceased taking warfarin early in the study period.

The research team then contacted the pathology laboratories that had claimed for payment from DVA for assessing veteran's INR results. Each laboratory was sent a copy of the relevant veteran's consent form and an explanatory letter detailing the

data requested (Appendix 2). Each laboratory then provided INR information to the research team.

Figure 10: Data collection process



3.2.4 Study population

This project aimed to investigate the current state of warfarin management in veterans taking warfarin and to assess the INR control of this population. The most common method for assessing INR control uses Rosendaal's linear interpolation method for calculating the proportion of time spent within the therapeutic range.[348] This calculation requires a set of test dates and INR results, with intervals no greater than eight weeks (56 days) between tests.[62] For this reason, the study population included veterans who had provided consent, had more than two dispensings of

warfarin in a six month period, and for whom INR results were obtained, with an average testing interval of less than 57 days.

3.2.5 Demographics

Demographic details were analysed for those veterans for whom INR results with an average testing interval of less than 57 days were available. The sex, age, state, remoteness,[349] number of recorded comorbidities and number of regular medications were determined for each veteran. The number of regular medications was obtained from the dispensing details in the 12 months following the first recorded dispensing of warfarin, and was defined by two or more dispensings in a six month period. As antibiotics with repeats are likely to have two dispensings in a six month period but not be regular medications, all medications with ATC codes commencing with 'J' were excluded from the analysis.[346] It is recognised that some veterans may have an indication for ongoing antibiotic therapy and as such this method may provide an under-estimation of the actual number of regular medications in this population.

3.2.6 INR control

The TTR was calculated using Rosendaal's linear interpolation method[348] for the study period. An INR target range of 2.0 to 3.0 was assumed for this analysis as specific diagnoses for the conditional requiring anticoagulation was not available for the majority of patients and a range of 2.0 to 3.0 is appropriate for most elderly patients.

Overall INR control, as defined by TTR, was determined for the study population. This was then further analysed by examining levels of control by state and region.

3.2.7 Handling of data

All data was treated confidentially and anonymously. The names of participating veterans were not stored with data files on computer.

3.2.8 Statistical analysis

All information was stored and analysed using SPSS 18.0 for Windows (SPSS Inc. Chicago, Illinois, USA). Demographic variables were compared using the following methods. Unpaired t-tests were used for normally distributed continuous variables; the non-parametric Mann-Whitney test was used for non-normal data. Categorical variables were analysed using the chi-square test. Fisher's exact test was used when at least one of the variables had fewer than five patients or events. One-way ANOVA with Bonferroni correction was used to compare three or more groups. Statistical significance was set at $p < 0.05$.

3.2.9 Ethical approval

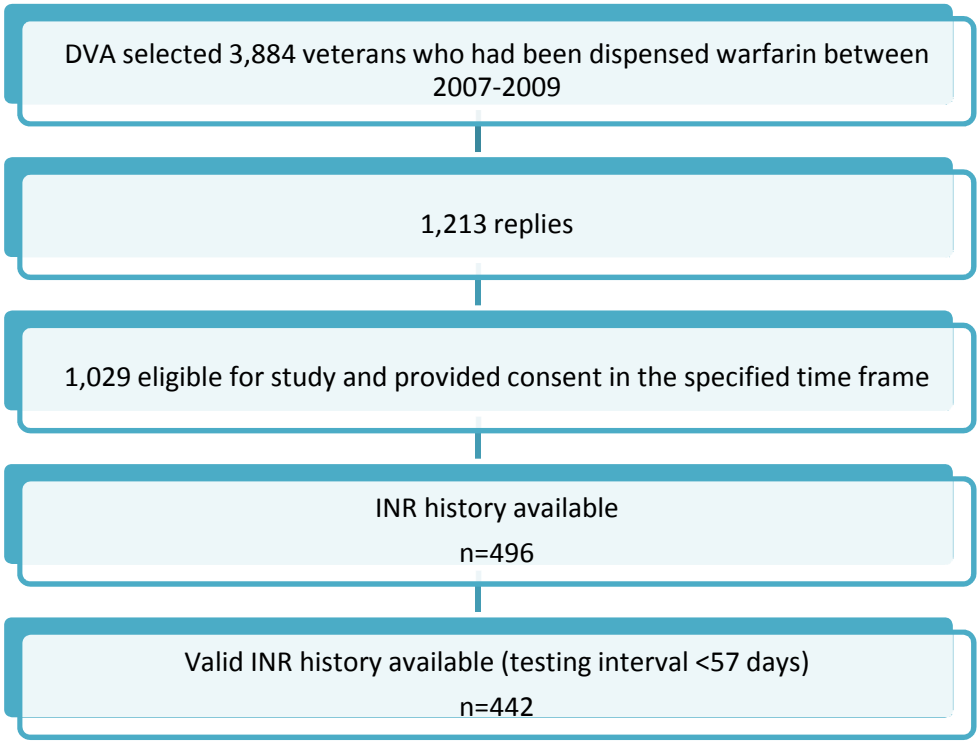
Ethical approval for this project was provided by the DVA Human Research Ethics Committee (E009-010) and the Tasmanian Health and Medical Human Research Ethics Committee (H0010963).

3.3 Results

3.3.1 Patient recruitment

The DVA selected 3,884 veterans according to the project methodology, from which the project team received 1,213 replies (31.2% response rate). A total of 1,029 who replied provided consent and were eligible for inclusion in the project. There was a total of 496 veterans for whom warfarin had been dispensed more than twice in a six month period and INR histories (of greater than one INR result) falling within the study period were available. INR histories with average testing intervals of less than 57 days were available for 442 (43.0%) of veterans included in the study cohort (Figure 11).

Figure 11: Recruitment flowchart of veterans



3.3.2 Patient demographics

The demographics of the study population are shown in Table 6.

Table 6: Veteran demographics

	Overall (n=442)
Male gender (%)	292 (66.1)
Median age (range)	82.7 years (55 – 93 years)
Median number of recorded comorbidities (range)	7.0 (1 – 28)
Median number of regular medications (range)	13.0 (1 – 58)
Number with a recorded diagnosis of AF (%)	113 (25.6)
Number with a recorded diagnosis of DVT (%)	81 (18.3)
State	
NSW (%)	200 (45.2)
SA (%)	36 (8.1)
ACT (%)	3 (0.7)
QLD (%)	28 (6.3)
TAS (%)	22 (5.0)
VIC (%)	111 (25.1)
WA (%)	42 (9.5)
NT (%)	0 (0)
Region	
Major city of Australia (%)	301 (68.1)
Inner Regional (%)	102 (23.1)
Outer Regional (%)	31 (7.0)
Remote Australia (%)	6 (1.4)
Very Remote Australia (%)	0 (0.0)
Unknown (%)	2 (0.5)

3.3.3 INR control

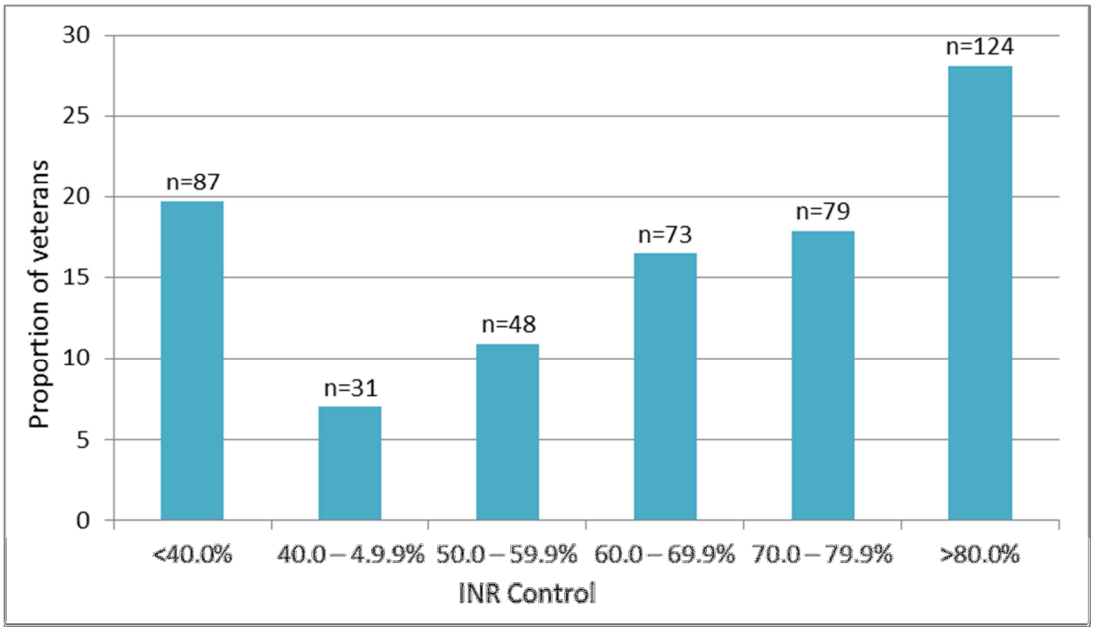
The study population comprised 442 veterans with average INR testing intervals of less than 57 days. The overall INR control data is summarised in Table 7. The mean testing interval was approximately 19 days and the mean TTR was 61.8%. Figure 12

shows a summary of the distribution of the mean TTR. Approximately 28% of veterans' mean TTR was over 80%, however, the mean TTR was below 60% for approximately 38% of veterans. Increased INR testing frequency (defined as fewer days between INR tests) was associated with increased TTR ($p<0.001$).

Table 7: Overall INR control

	Overall (n=442)
Mean number of tests in study period (range)	40.6 (37.7 – 43.5)
Mean testing interval in days (range)	19.4 (18.3 – 29.5)
Mean duration of testing in days (95% CI)	705.8 (668.3 – 743.3)
Mean percentage TTR (95% CI)	61.8 (59.4 – 64.2)
Mean percentage time below therapeutic range (95% CI)	27.8 (25.3 – 30.3)
Mean percentage time above therapeutic range (95% CI)	10.4 (9.0 – 11.7)

Figure 12: Mean TTR distribution



There was no significant difference in the INR control between male and female veterans, $p = 0.730$ (Table 8). Nor was there a significant difference in the INR control between veterans of varying age groups, $p = 0.544$ (Table 9).

Table 8: INR control by gender

Gender (n)	Mean TTR (95% CI)	*p*-value
Male (292)	61.5 (58.4 – 64.7)	0.730
Female (150)	62.4 (58.5 – 66.37)	

Table 9: INR control by age group

Age group (n)	Mean TTR (95% CI)	*p*-value
50-59 years (6)	63.9 (33.1 – 94.7)	0.544
60-69 years (18)	54.5 (40.9 – 68.2)	
70-79 years (71)	64.4 (58.8 – 70.0)	
80 years and above (347)	61.8 (59.4 – 64.3)	

A one-way between-groups analysis of variance was conducted to explore the impact of the number of regular mediations on INR control. Veterans were divided into four groups according to their recorded number of regular medications (≤4, 5-7, 8-10, ≥11). There was a statistically significant difference in TTR between the four groups: F (3, 438) = 3.42, p = 0.02. TTR decreased with increasing number of medications (Figure 13). Post-hoc comparisons using the Tukey HSD test showed no significant differences between the groups. The effect that the number of comorbidities has on INR control was not investigated due to the high number of veterans without comorbidities recorded.

Figure 13: INR control by regular medications

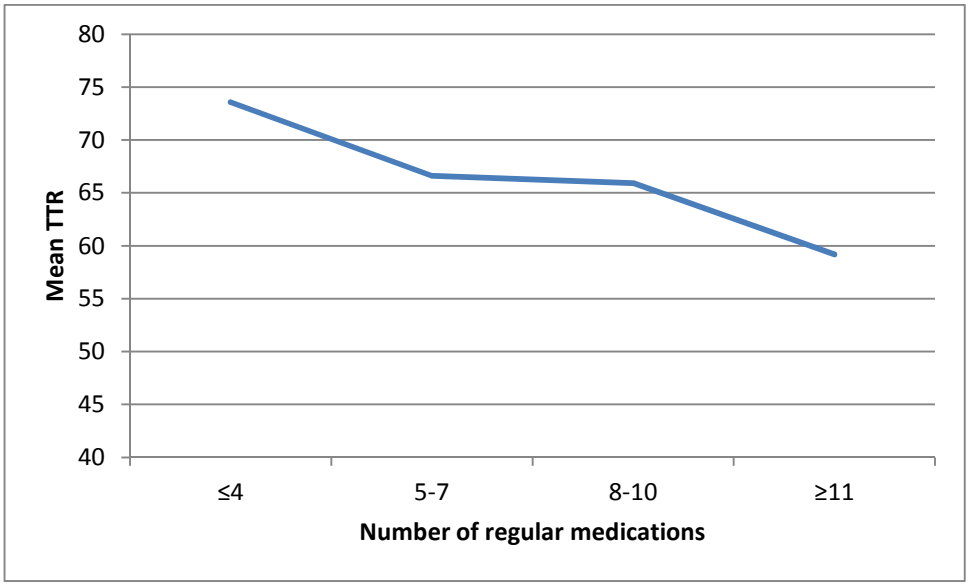


Table 10 shows a breakdown of the TTR for Australian states and territories. There was no significant difference in TTR between the Australian states and territories where veterans included in the study reside, F (6, 435) = 1.733, p = 0.112.

Table 10: INR control by state

State or territory (n)	Mean TTR (95% CI)	*p*-value
NSW (200)	63.4 (60.0 – 66.9)	0.112
SA (36)	49.5 (40.9 – 58.2)	
ACT (3)	46.9 (36.6 – 57.2)	
QLD (28)	62.0 (51.6 – 72.4)	
TAS (22)	60.7 (50.2 – 71.3)	
VIC (111)	62.5 (56.9 – 68.1)	
WA (42)	64.7 (57.5 – 71.8)	
Overall (442)	61.8 (59.4 – 64.2)	

Table 11 shows a comparison of mean TTR by region. Significant differences were found between control in different regions, F (3, 436) = 5.586, p = 0.001. Mean INR control in cities and inner regional areas was found to be significantly better than that in outer regional areas of Australia. Post-hoc testing, using Bonferroni

correction, demonstrated significant differences exist between the pairs 'Major Cities and Outer Regional' and 'Inner Regional and Outer Regional' (Table 12). There were too few veterans listed as residing in Remote Australia (n=6) to obtain meaningful results from comparing this region.

Table 11: INR control by region*

Region (n)	**Mean TTR (95% CI)**	***p*-value**
Major City of Australia (301)	63.9 (61.0 – 66.8)	**0.001**
Inner Regional (102)	62.1 (51.0 – 67.1)	
Outer Regional (31)	44.7 (33.6 – 55.8)	
Remote Australia (6)	51.1 (29.2 – 73.0)	
Total (440)	61.9 (59.5 – 64.4)	

* The region for two veterans was unknown.

Table 12: INR control by region – post-hoc analysis

Region/ *p*-value	Major City of Australia	Inner Regional	Inner Regional	Remote Australia
Major City of Australia	-	1.000	**0.001**	1.000
Inner Regional	1.000	-	**0.006**	1.000
Outer Regional	**0.001**	**0.006**	-	1.000
Remote Australia	1.000	1.000	1.000	-

Findings in **bold** indicate statistical significance.

There was no significant difference between the frequency of INR testing between regions, F (394,45) = 0.858, p = 0.776 (Table 13).

Table 13: Testing frequency by region*

Region (n)	**Mean testing frequency in days (95% CI)**	***p*-value**
Major City of Australia (301)	18.7 (17.4 – 20.0)	0.776
Inner Regional (102)	21.5 (19.0 – 23.9)	
Outer Regional (31)	19.0 (13.7 – 24.3)	
Remote Australia (6)	18.4 (1.9 – 35.0)	
Total (440)	19.4 (18.3 – 20.5)	

* The region for two veterans was unknown.

3.4 Discussion

The veteran population included in this study was very similar to the overall veteran population of Australia. However, this study included a higher proportion of males (66% versus 58%) and the participants were generally older than the general veteran population (85% of the study population was over 70 years versus 70% of the general population). It is likely that this can in part be explained by the study population being people who take warfarin, the most common indication for which is AF, and the higher prevalence of AF in older men.[111] The veterans in this study were spread slightly differently by state in comparison to the overall veteran population; however, the proportion from the eastern states was essentially the same (77.3% for the study group versus 79.5% for the general veteran population) suggesting similar access to services as the general veteran population.

There is one key difference that is evident in the model of usual care warfarin management between Australian states and territories. In the majority of states the patient's GP is the primary provider of anticoagulation management, assessing INR results and advising on dose requirements. In Victoria and Queensland this role is often assumed by a pathology provider, who will assess the result and provide feedback on dosage adjustments directly to the patient. Importantly, in this study the proportion of veterans from Victoria and Queensland, in combination, was very similar between both groups (41.4% for the study group versus 45.5% for the general veteran population). This difference in usual care practices is often thought to be a difference in management models which could affect INR control between states. No significant difference was seen in the INR control between states, suggesting that the overall INR control of the study population may be representative of the overall control in Australia, independent of state.

A significant difference was found between the INR control of those veterans residing in cities and inner regional areas when compared to those in outer regional areas. Little data is available in the literature relating to the differences in INR observed in areas with differing degrees of rurality. However, the finding is perhaps not unexpected. Regional areas of Australia receive substantially less federal health funding per capita than their urban counterparts,[350] and the remoteness index by which participants were classified takes into account access to healthcare resources.[351] However, access differences cannot fully explain this difference in control between more metropolitan areas and outer regional areas as there was no significant difference observed between the INR testing frequencies in each region. This would suggest that access to INR testing, if not other healthcare resources, is similar across the country. It is likely that factors other than those considered in the data presented here have a role to play in explaining the difference in INR control observed.

As previously discussed, the use of warfarin requires regular monitoring of the INR to maintain levels of anticoagulation that are both safe, in terms of minimising the risk of bleeding, and effective, in minimising the risk of thromboembolic events.[12] Maintaining the INR within the therapeutic range is the key to achieving safe and effective use of warfarin, and the higher the TTR the better the outcomes that can be expected from therapy.[54] INR control was found to decrease with increasing numbers of concurrent medications. This is to be expected given the increased risk of interacting medications and the increasing potential for poor compliance which results from taking a greater number of medications.[352]

INR data was available for 43% of veterans included in this study. The mean TTR was 61.8% and was not influenced by state of residence. This suggests that the model of management, office-based management by a physician versus management

by a pathology laboratory, did not influence overall INR control in this patient population.

The level of INR control demonstrated by veterans in this study compares very well to other studies of INR control. In a large systematic review, the INR control of 50,208 patients from 67 published studies were compared.[56] Overall, the average TTR was found to be 63.6% across all groups. This was slightly lower than in randomised controlled trials where the TTR was 66.4%, but higher than the TTR of 56.7% seen in community practice studies.[56] The review then separated the community practice results to exclude those which included self-monitoring to look at the INR control of those people managed purely by what we would consider community-based usual care. In this setting the TTR was as low as 50.0%. The INR results of veterans included in our study would be those of patients who were not undertaking self-monitoring as included results were provided by pathology laboratories. Self-obtained results would be held by the patient and as such would not have been available for analysis. In view of this, the TTR of 61.8% achieved by Australian veterans managed by community-based usual care models rates very well against what is seen in many other countries.[62] Additionally, 28% of veterans included in the study achieved TTRs of 80% or above, control which could be classified as excellent.[62]

To date, the largest published data on INR control in an Australian setting comes from the Point of Care Trial (PoCT).[68-70] The INR control of the PoCT usual care group during the intervention was better than that observed in the veteran population of this study, with post-hoc analyses suggesting a TTR of 68%.[71] However, it should be noted that the PoCT participants represented a younger cohort whose primary care physicians were aware of their participation in a research study. This awareness is likely to have impacted on the level of care

provided by the physician, potentially improving their therapeutic control. As such the results from the control group during the intervention phase of the PoCT cannot be taken as truly representative of the control of a group of patients undergoing usual care.

Very little other published data is available on the anticoagulation control of the Australian population taking warfarin, making this study of the INR control of veterans the largest set of data available on the TTR of patients managed by standard community-based care in Australia to date.

However, it has been suggested that high quality anticoagulation management should be defined as achieving a TTR of between 60-70%.[61, 62] The data from the veterans in this study showed 37.6% of participants had TTRs below 60% and over half (54.1%) achieved TTRs of less than 70%. Despite demonstrating INR control in Australian veterans equivalent to, or better than, that seen in other studies of community-based patients in Australia, there is still significant room for improvement in the quality of anticoagulation control in this population.

Australian veterans could be viewed as potentially receiving a higher level of primary care than the average Australian patient. The DVA targets both the veterans and their GPs with educational campaigns to improve the quality of care for veterans through a program known as Veterans' Medicines Advice and Therapeutics Education Services (Veterans' MATES).[353] The warfarin module of Veterans MATES was distributed in November 2008, during the study period. This may have had an impact on the level of attention veterans and their GPs paid to warfarin around this time, and may have impacted on the level of INR control achieved. As such, it is possible that the INR control of the general Australian population is lower than that of the veterans in this study, further supporting the need for strategies to improve the quality of anticoagulation control in Australia.

3.4.1 Limitations

In order to obtain INR histories for included patients in the study, the investigators were required to obtain consent from veterans. This meant that it was not possible to obtain information from veterans who had died either during the study period or in the time following the study period prior to the DVA mail-out, and excluded veterans who were readmitted to hospital with a major bleeding or thrombotic event and subsequently died. Therefore, we were not able to investigate the data of the entire veteran cohort who were taking warfarin during the study period. It is possible that the more seriously ill veterans, and perhaps those most likely to suffer from adverse events related to warfarin or labile INRs were not included as a result of this methodology.

The data available from the DVA was limited in respect to the documentation of comorbidities, which meant that it was impossible to determine the indication for warfarin from the data available. Therefore, a target INR of 2.0 to 3.0 was assumed for all veterans. However, if anything, this would have resulted in an under-estimation of the TTR rather than an over-estimation of the degree of INR control. Despite the inclusion criteria being based on the regular dispensing of warfarin and the requirement for regular INR monitoring for people taking warfarin, data were only available for approximately 43% of the included veterans. There are a number of potential reasons for this. In some cases, the pathology provider did not comply with the joint request from the research team, the DVA and the veteran for the data to be released. Some providers attempted to charge an unreasonable fee for this data to be released, seemingly far outweighing the actual costs of collating the data requested. In other cases, the pathology providers linked to the veteran in the DVA database did not hold any INR data on the veteran. The pathology provider, in some cases, only held a proportion of the INR data available; the veteran may have

changed provider or office-based INR testing was used (in which case it was not available to the pathology provider). It was not possible to identify which veterans may have received office-based point of care INR testing during the study period and it is therefore unknown whether their INR control is comparable to that of the veterans included in this study. It may also be possible that veterans who participated in the study had a different level of INR control that those who did not participate.

3.4.2 Conclusion

The average level of INR control in the study cohort was good, achieving the overall goal of a TTR of above 60%, and it was comparable to TTRs achieved in recent RCTs, which generally involve a younger, healthier cohort. However, these results suggest there remains room to improve the INR control of Australian veterans taking warfarin. Methods to improve INR control should be investigated further. Such investigations form the basis for the remainder of this thesis.

Chapter 4 : Development and Utilisation of an Online Anticoagulation Resource

4.1 Purpose of the study

Education has been identified as an important tool in reducing complications of therapy through improving patient understanding,[132] and as such improving access to education is a key factor in improving patient outcomes. Despite the importance of educational interventions involving face to face counselling, there are often difficulties associated with patient understanding and recall.[159] Complementing traditional counselling with the provision of online resources has benefits for further increasing health knowledge, giving patients the opportunity to reinforce their learning in a convenient and comfortable environment.[167] Despite the recognised benefits of online resources, a lack of accessible, high quality health information available for patients requiring anticoagulation therapy exists.

This study aimed to describe the development and utilisation of an online resource, www.anticoagulation.com.au, to provide accessible anticoagulation information to patients and health professionals. It also aimed to describe an online INR monitoring platform and patient experiences using this platform.

4.1.1 Context

The website was initially designed as part of the Pharmacist-Based Model Enabling Patient Self-Monitoring of Warfarin study as a source of information and tools for participants to use as part of the implementation of a pathway for PSM. The role of the site grew independently of the project, seeing promotion of the site to all community pharmacies in Australia. As part of The Role of Community Pharmacy in Post Hospital Management of Patients Initiated on Warfarin: Patient Self-Monitoring Phase study, the site was redeveloped. The redevelopment included updating the content, improving the aesthetics and usability, and incorporating additional

functionality. The additional functionality enabled people taking warfarin to register with the site and log-in and record INR results. Patients in the PSM phase of the project were recruited to test an advanced form of this recording platform which incorporated electronic communication of INR results between patients and their GPs.

The concept of the website was conceived prior to the author becoming involved in the Pharmacist-Based Model Enabling Patient Self-Monitoring of Warfarin study. The author was responsible for designing the hierarchy of information storage for the website. She also wrote all the information content of the site, which was then reviewed by the research team. The study was designed by Luke Bereznicki, Gregory Peterson and the author. It was designed to be mainly descriptive in nature, to explore the development and utilisation of the resource. The additional functionality was designed by Luke Bereznicki and the author. All development of the website software was outsourced to contractors.

4.2 Methods

4.2.1 Development of www.anticoagulation.com.au

The website (www.anticoagulation.com.au) was developed to promote PSM and the safe use of warfarin in Australia, to provide anticoagulation information for all interested people and to house educational tools. The website was designed to provide both patients and health professionals with information and educational resources regarding anticoagulation topics, primarily focussed on warfarin therapy. It aimed to be both a comprehensive and reliable online resource, particularly for patients interested in PSM.

The author attended a website usability course conducted by Hiser Pty Ltd (www.hiser.com.au), a company specialising in user interface design and user experiences. This course assisted in approaching the design process from a perspective which was likely to produce the most successful and usable final product.

A user-centred design approach was adopted, involving identifying the goals of the website and the likely user groups and defining their needs. This approach encourages a design which:

- Makes it easy to determine which actions are possible at any moment;
- Makes the conceptual model of the system visible to the user, including alternative actions available and the results of any actions taken;
- Makes it easy to evaluate the current state of the system; and
- Follows intuitive mappings between intentions and the required actions.[354]

The user-centred design process ensured fundamental content areas were identified and developed. The Project Advisory Group was consulted during the development process. This stakeholder consultation process was crucial to ensure the information available from the website was both relevant and appropriate to the target audience.

A number of designs were trialled with the Project Advisory Group to identify preferred layouts and navigation options before a final design was settled upon. The home page was designed to accommodate the site identity and mission, the site hierarchy, a search function, and an overview of the site's content. The remainder of the site was designed to enable easy, intuitive navigation throughout the content, aided by the inclusion of cross-referencing of information throughout the site. The project team enlisted the assistance of a professional web developer to produce the framework for the site.

Heuristic evaluations involve an evaluator inspecting an interface, or a description of an interface, with the view to identify any usability problems to enable solutions to be found early in the design process.[355] Heuristic evaluations were undertaken by the author and the Project Advisory Group throughout the design phase of www.anticoagulation.com.au to identify theoretical usability issues before the site was launched. These evaluations identified a number of minor usability issues which were able to be modified and the issues were resolved early in the testing process. Modifications were primarily made to the menu functions, to replace missing links to downloads and external pages, and to ensure that cross-referencing of information within the site worked effectively.

To ensure the aim of supplying reliable health information was achieved and recognised, the website was submitted to and obtained Health On the Net HONcode certification. This certificate allows a site to demonstrate its intention to contribute

to quality medical information.[356] To gain certification the website needed to have considered the transparency of ethical aspects of health information provision. These covered the credentials of the authors, the date of the last modification of clinical documents, references for clinical information, statements regarding the confidentiality of data, and the site's policies regarding funding and advertising.[356]

Content was written according to guidelines for writing patient health information,[357] with an emphasis on a patient audience. Readability evaluations of health information contained on the site was measured using the Flesh-Kincaid Grade Level test. Information presented included simply worded but detailed information on warfarin, including how warfarin works as well as a range of information on taking warfarin safely and effectively. Indications for warfarin and other anticoagulant agents were also discussed, along with options for monitoring therapy. Other features of the patient-focussed design were frequently asked questions and a glossary of anticoagulation-related terms.

A range of downloadable resources were also produced for inclusion on the website following the same guidelines for writing patient health information. These included:

- Patient information leaflets (such as the 'Warfarin and you' Information Leaflet (Appendix 3), a One Page Guide to Warfarin Treatment (Appendix 4) and quarterly newsletters(Appendix5));
- Patient anticoagulation resources (such as a Warfarin ID Card (Appendix 6), INR Record Book (Appendix 7), and an INR Record Form (Appendix 8));
- Patient self-monitoring resources (such as a Patient Self-Monitoring Diagram (Appendix 9) and a Self-Monitoring INR Record Book (Appendix 10)); and

- Health professional resources (such as a Counselling Checklist (Appendix 11) and a Pre Self-Monitoring Assessment Tool (Appendix 12)).

All content and resources underwent review by the Project Advisory Group as well as readability evaluations to ensure an appropriate language level of content for the general population. Accessibility issues were also taken into account to ensure equitable access to the site for all users. The site and downloads were rated at a reading grade level 6. The structure of the website content can be seen in Figure 14 and Figure 15.

Figure 14: www.anticoagulation.com.au content structure (i)

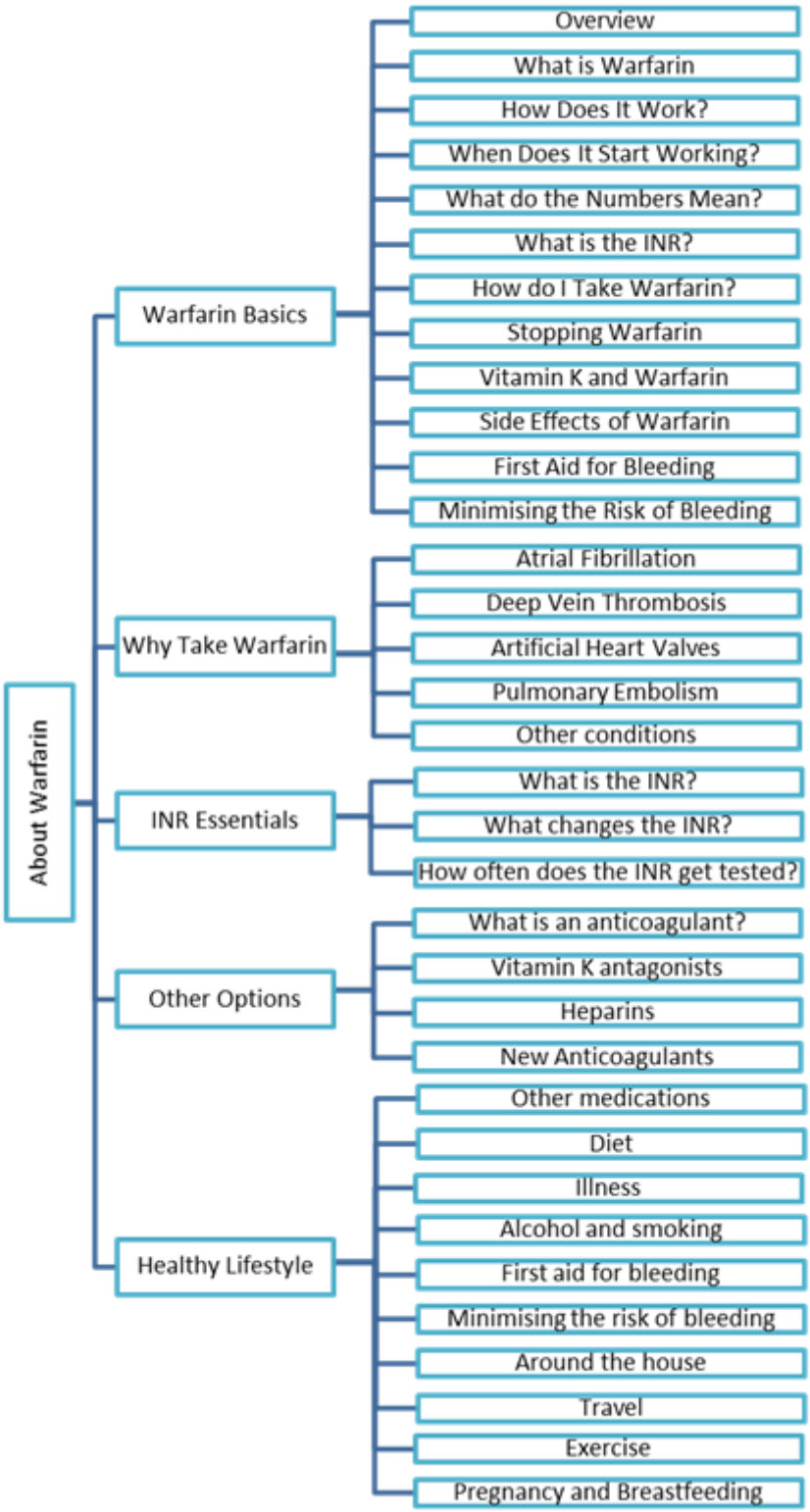
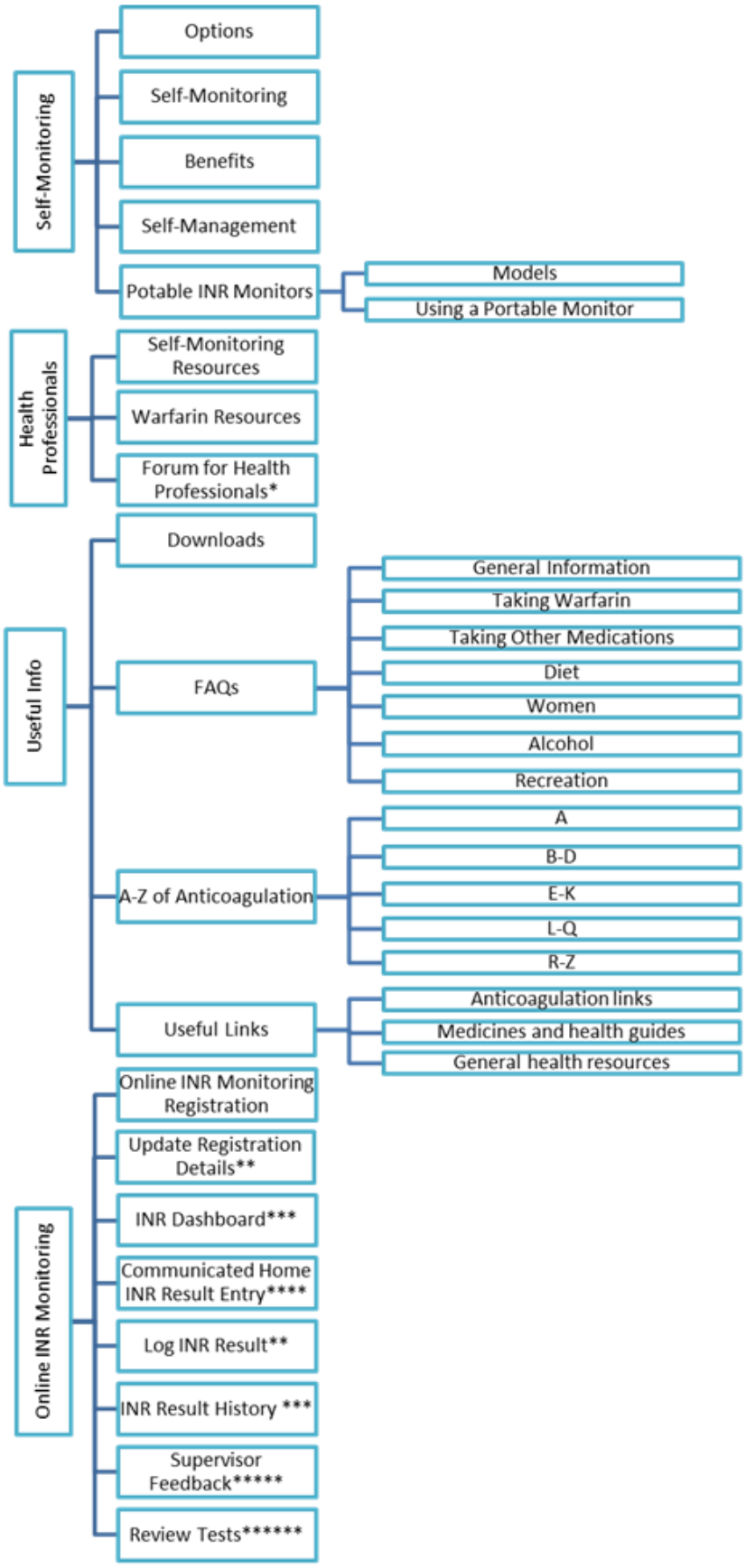


Figure 15: www.anticoagulation.com.au content structure (ii)



The site was launched through Australia's 5000 community pharmacies in October 2008. The launch was supported with promotion in pharmacy media and the distribution of promotional materials to all pharmacies. Pharmacies were provided with tools to promote the resource to their patients (Appendix 13).

Examples of the original live design of www.anticoagulation.com.au are shown in Figure 16, Figure 17 and Figure 18.

Figure 16: Original www.anticoagulation.com.au homepage

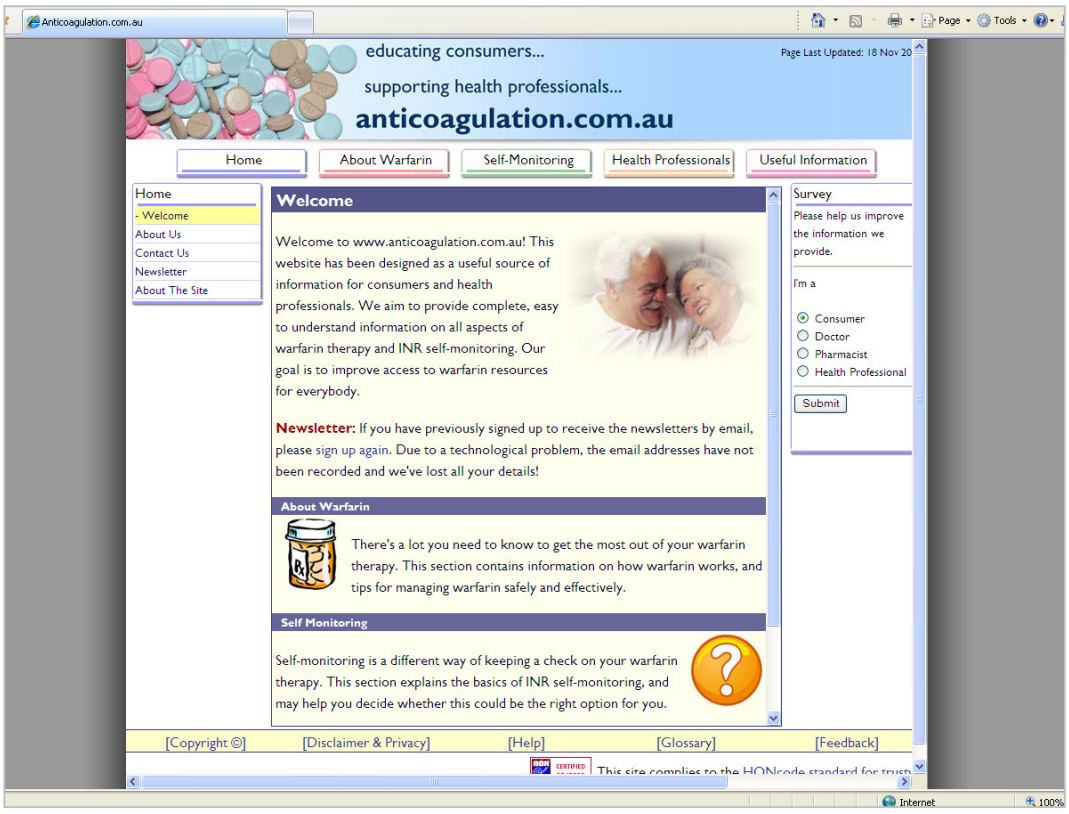


Figure 17: Original www.anticoagulation.com.au contents example (i)

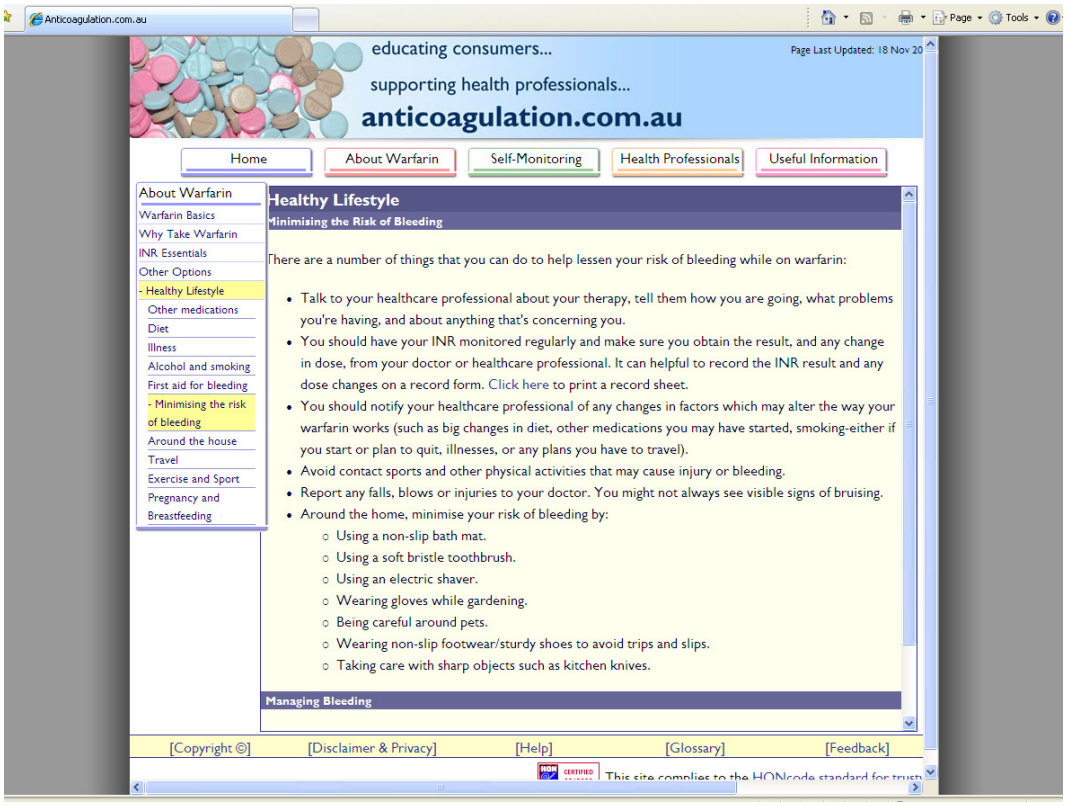
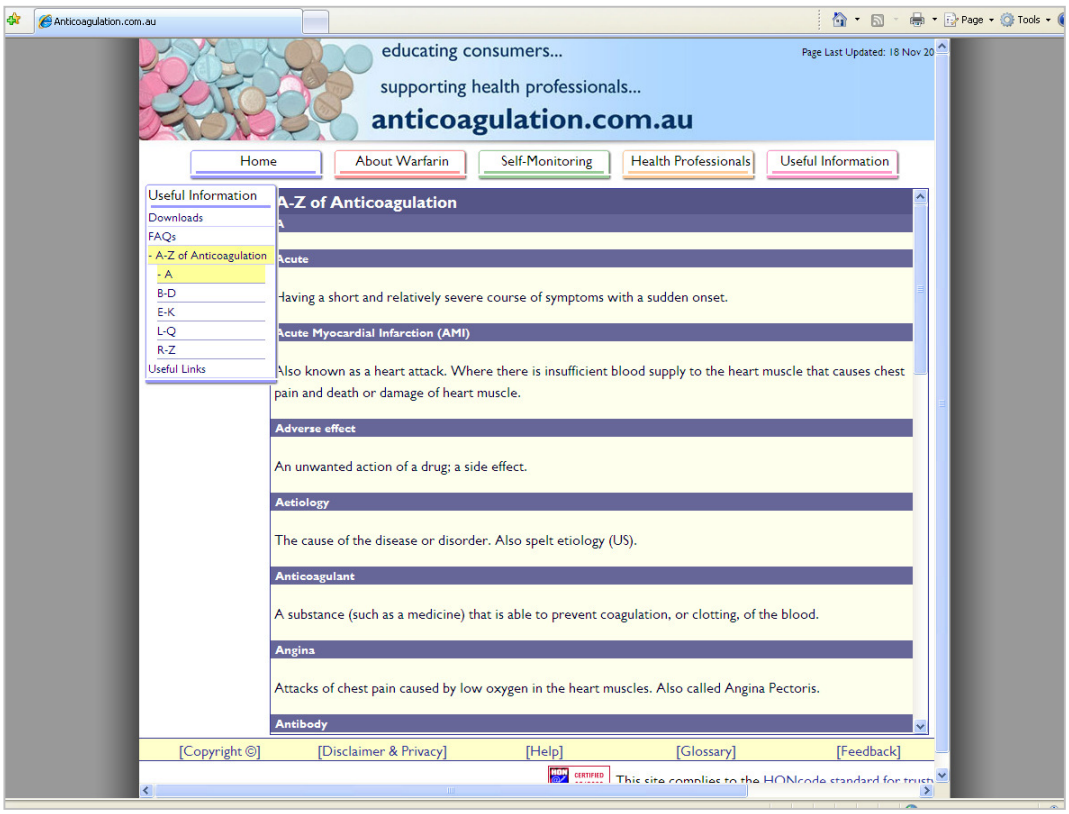


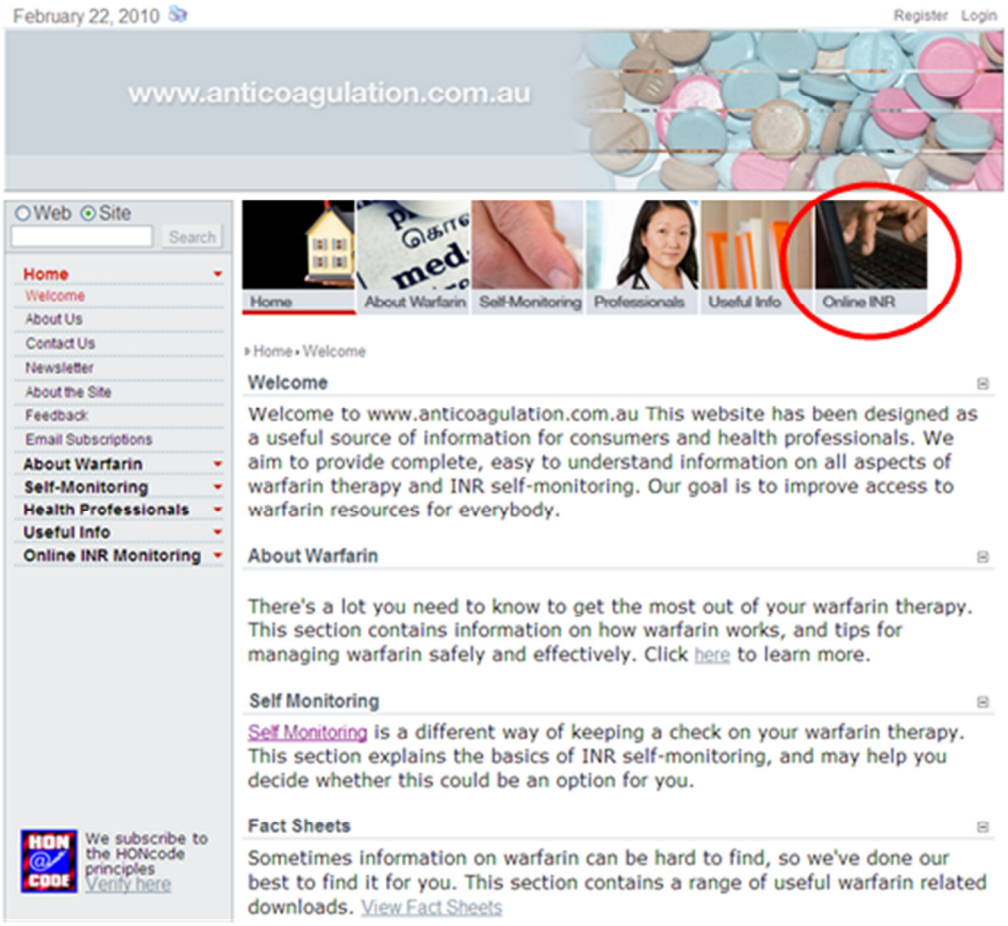
Figure 18: Original www.anticoagulation.com.au contents example (ii)



4.2.1.1 Online monitoring platform

After the initial 12 months, the website underwent significant redesign as part of The Role of Community Pharmacy in Post Hospital Management of Patients Initiated on Warfarin: Patient Self-Monitoring Phase project. It was relaunched with a new look and additional functionalities (Figure 19 and Appendix 14). The most important of these was the addition of an online recording function, where registered users could record their current doses of warfarin and their recent blood test results (Appendix 14a). Test results were represented in both tabular form and graphically to enable users to easily track their progress in regards to control of therapy. The home-monitoring platform was developed for the use of self-monitoring patients who were capable and willing to communicate their INR results to their GP via the internet. Patients and GPs received training by accredited pharmacists regarding the use of the secure website to enable the communication of INR results and incident reports between them.

Figure 19: www.anticoagulation.com.au



(Note: Patients entered the online INR platform via the link at the top right (circled).)

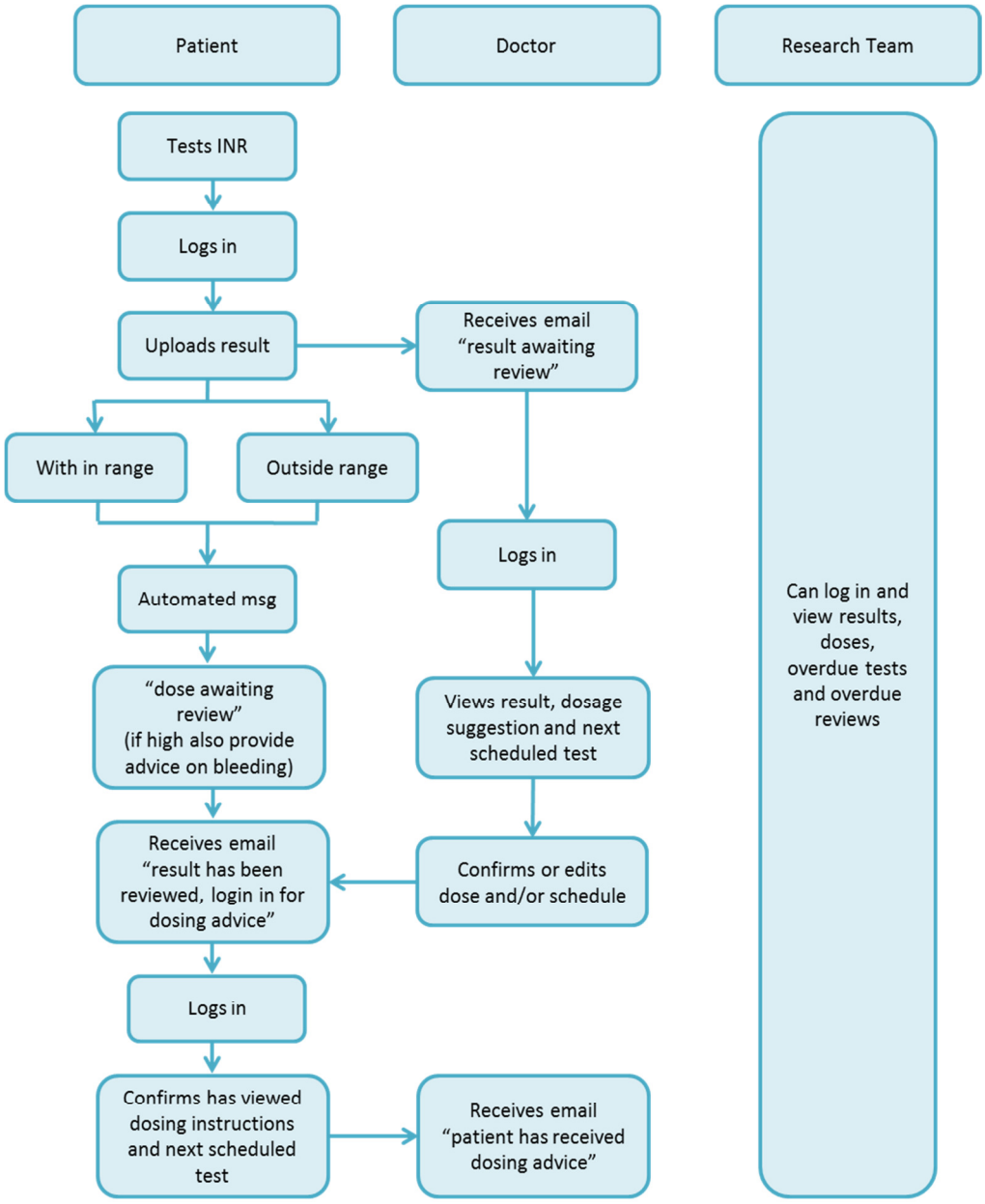
The process of INR reporting and review can be summarised as seen in Figure 20:

1. INR results obtained by the CoaguChek®XS were entered manually into a password-protected internet repository by the participant.
2. The website generated an email free of sensitive details which was sent to the GP to alert them that there was an INR result for them to review.
3. The GP logged onto the website to view the patient's details. They could then make an on-line recommendation based on the INR and stored history.
4. The website generated an email prompting the patient to log in and review the dosage instructions.

5. On reviewing the GP feedback, the patient acknowledged the feedback, prompting another email to the GP to notify them that their patient had received their advice. This email completed the feedback loop for the testing procedure.

The steps involved in this process can be seen in Appendices 14b, 14c, and 14d.

Figure 20: Pathway for INR review via the online platform



The website had additional inbuilt supervisor capabilities to enable a patient's community pharmacist, or another medical supervisor, to access the online INR history with the patient's consent.

Patients who did not use the web-based platform in this self-monitoring project continued to contact their GP surgery via telephone or email to communicate their INR result.

4.2.2 Data collection

The utilisation analysis was performed on website usage data collected over the 12 months between October 1, 2008, and September 30, 2009. This period started with the month in which the website was launched and concluded with the last month before the revised version of the site was launched.

Raw data were collected and exported in a variety of formats using cPanel VPS Optimized (cPanel Inc, Houston, TX, USA). Noisy data, such as that created by web crawlers, was eliminated from the analyses.

4.2.3 Web utilisation

The following information was used to measure the utilisation of www.anticoagulation.com.au.

- Page view: A page view is recorded each time a user visits a web page.
- Visits: A visit describes the interaction between a visitor and the website. A single visit may include multiple page views.
- Unique visits: A unique visit is determined by recording the internet protocol address of each user. A single unique visitor may account for multiple visits.

- Geographic statistics: These represented locations across the world from which pages of the website were accessed.
- Duration of stay: The duration was recorded as an average duration of stay per visitor to the site.
- Information downloads: This reported the number of downloadable information leaflets viewed by visitors to the website.
- Website referrals: This assessed how individuals were referred to the website, whether via a direct bookmark entry, search engine referral or via referral from another external webpage.

4.2.4 Feedback

A survey was embedded within the site to collect demographic information on the visitors to the sites and to enable user feedback on various aspects, including design and content, as well as suggestions for improvements. Emails sent to the website address were also evaluated as feedback and utilised in the evaluation process and redesign processes.

4.2.4.1 Online INR monitoring platform feedback

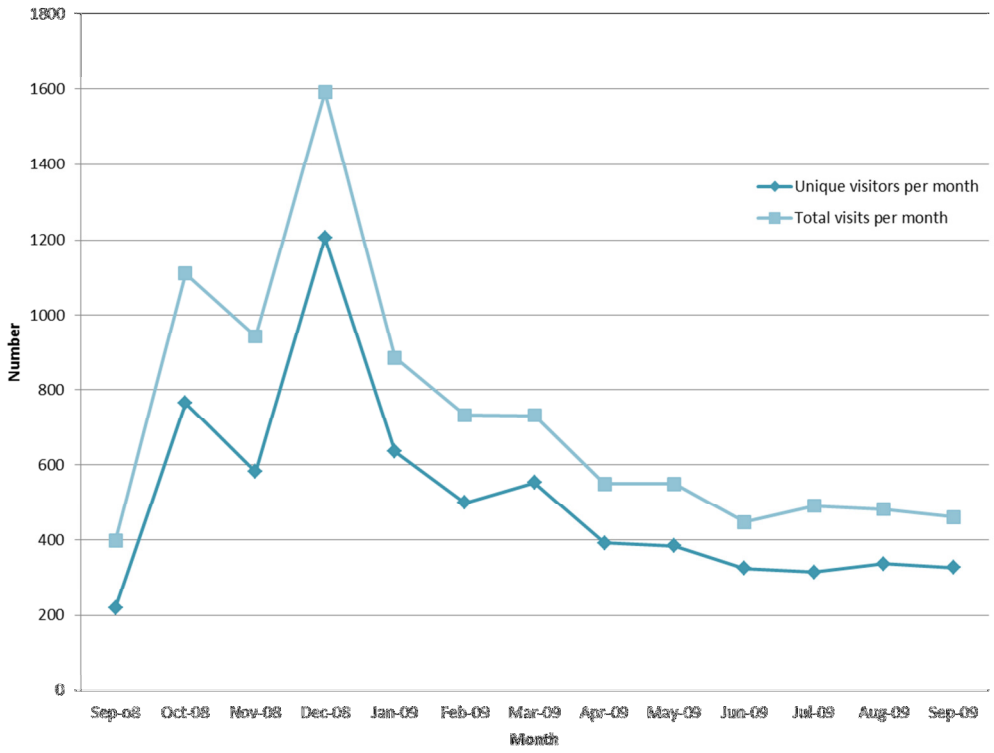
GPs and patients who consented to using the online platform for communication of INR results completed an evaluation questionnaire on their experiences with the website. Interviews were also conducted with patients who utilised the online INR monitoring platform as part of the PSM phase and the responses were qualitatively analysed.

4.3 Results

4.3.1 Web utilisation

Between October 1, 2008, and September 30, 2009, the www.anticoagulation.com.au website received 8,974 visits from 6,321 unique users. Users visited an average of 1.4 times, resulting in a total of 249,607 page views over the 12 months. As the promotional material from the launch was disseminated, the number of visits per month more than doubled (from 399 to 1110 visits per month). This increase was sustained for a number of months before the number of visits returned to around 500 visits per month in April 2009 (Figure 21). The pattern of unique visitors closely followed that of the total number of visits per month.

Figure 21: Site traffic per month

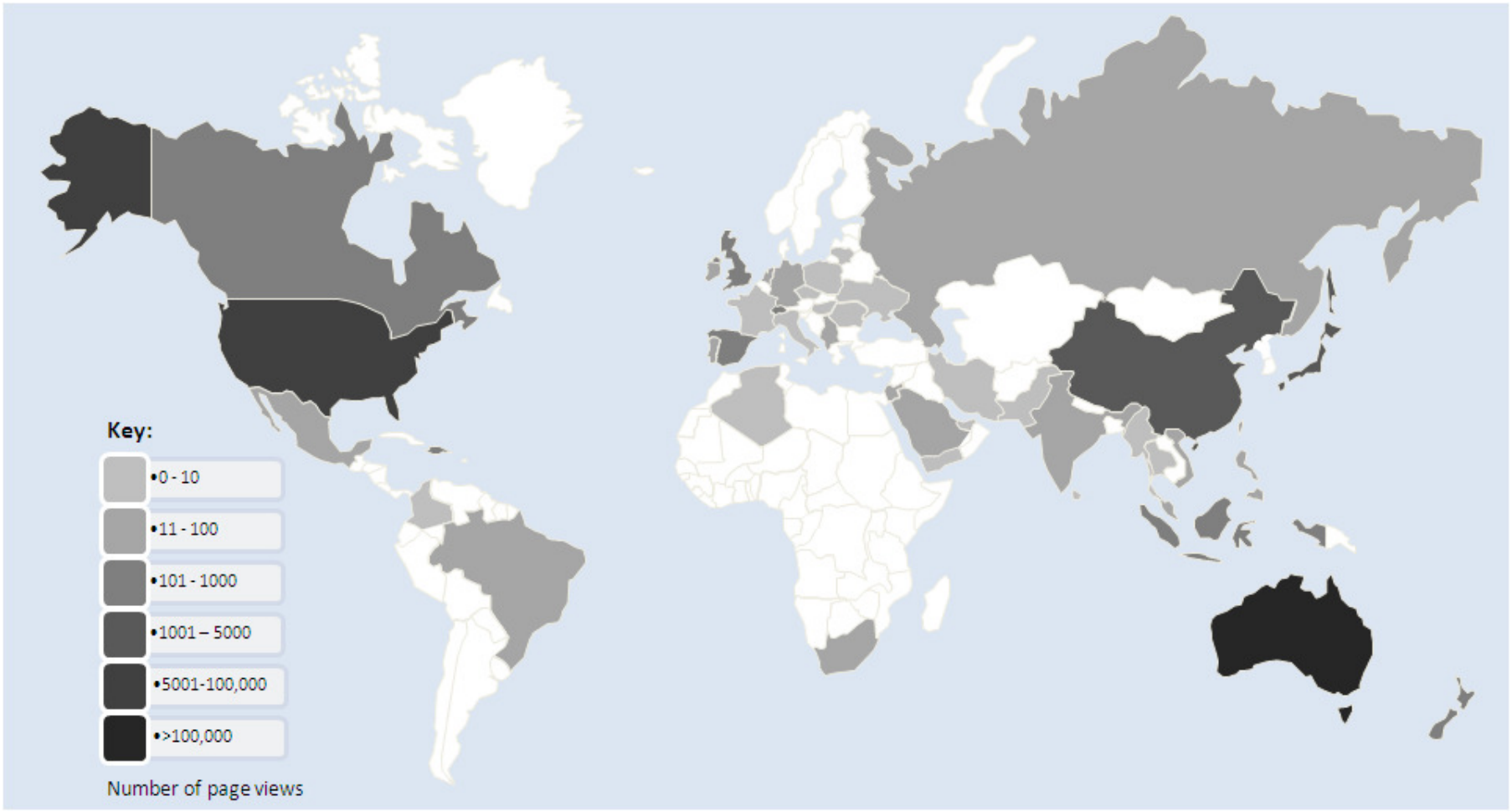


Of the visits, 92.8% originated from direct address entries, bookmarks or links in emails, 5.8% were referred by internet search engines, and 1.3% was referred by

websites other than search engines. The most common referring search engine was Google, accounting for 83.5% of search engine referrals.

Geographic distribution of page views showed that Australians were responsible for the majority of traffic. However a large portion of page views, totalling 40.3% of all page views in this period, originated from more than 50 foreign countries, as illustrated in Figure 22.

Figure 22: Geographic density of page views



Users stayed at the website for an average of 462 seconds (7.7 minutes) per visit. The downloadable resources were popular amongst visitors, with 6,232 resources being accessed during the 12 month period (Table 14).

Table 14: Number of resources downloaded

Downloadable Resource	Number downloaded
'Warfarin and you' information leaflet	1701
One page guide to warfarin treatment	1015
Warfarin ID card	883
INR record book	702
INR record form	678
Pharmacist counselling checklist	475
Self-monitoring diagram	378
Newsletters	211
Self-monitoring INR record book	176
Other	13

4.3.2 Feedback

A small volume of feedback was received via the embedded survey and by emails to the site administrator. Feedback was generally positive, with comments including:

"impressive";

"really clever thinking"; and

"the website is great – easy to use and very clear".

The number of completed feedback forms was too low to enable reporting and analysis of users' opinions of specific aspects of the site.

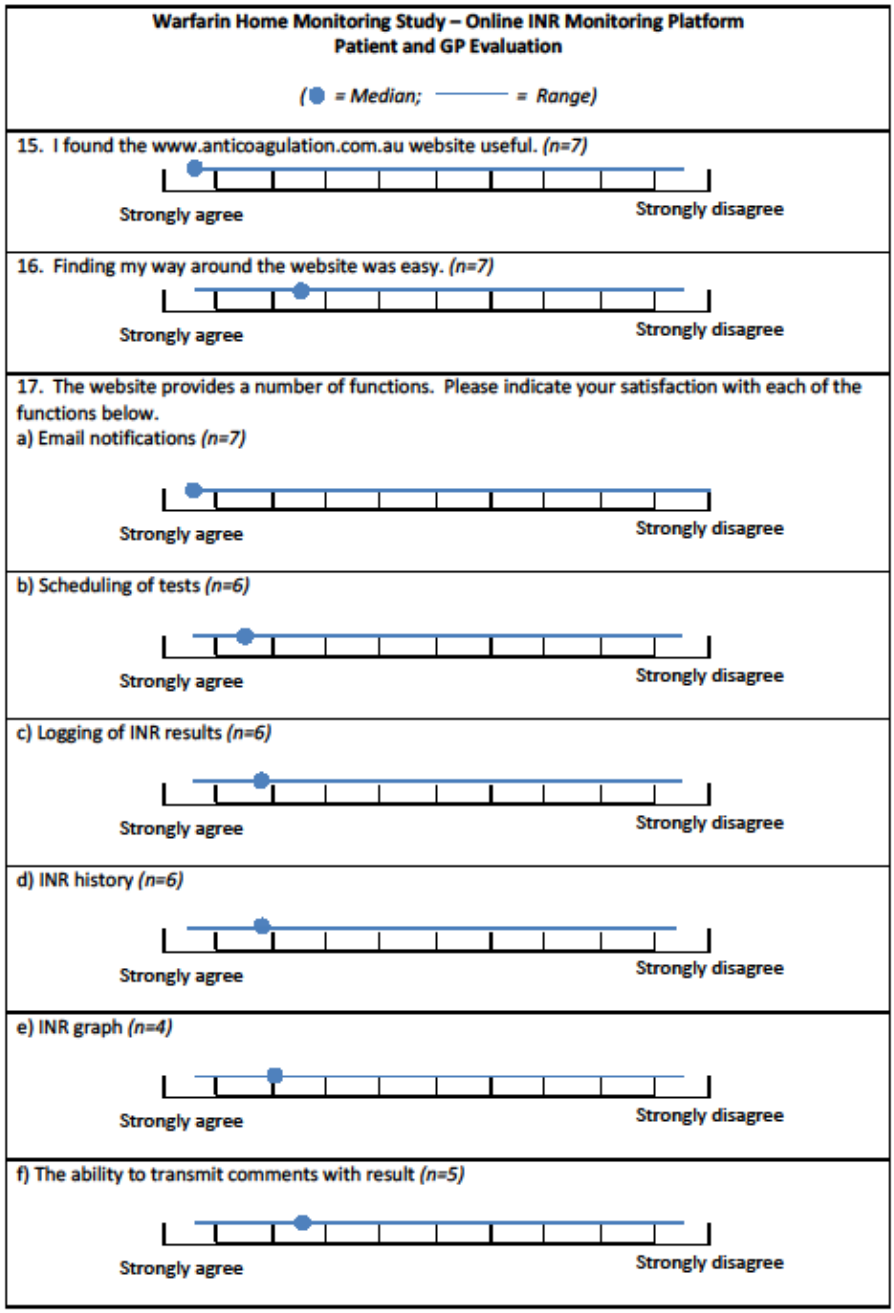
4.3.2.1 Online INR Online INR monitoring platform

All participating patients were invited to trial the online platform. Seven patients and their GPs were successfully recruited to use the online INR monitoring platform and received additional training from an accredited pharmacist on the use of this platform. Completed questionnaires were received from four patients and three GPs.

Patients and GPs generally expressed high levels of satisfaction with the website and the ability to transmit INR results. A visual summary of their responses is shown in Figure 23. The website was rated as easy to use and to navigate, and all the functions the website provides received high rating also.

There was no significant difference found between the INR control of those patients who utilised the web-based monitoring platform and those who did not.

Figure 23: Visual summary of online INR monitoring platform feedback



4.3.2.1.1 Qualitative responses

The online INR monitoring platform was also raised in interviews with self-monitoring participants (described in detail later in Part Three of the thesis). Qualitative feedback was received from all seven patients who utilised the web-based platform. Pseudonyms are used to identify the patients whose words are used in the quotations. For details on the demographic details associated with each pseudonym, please refer to Table 33.

Most feedback received was positive, with some participants describing the website as a great idea, which was simple to use:

> *I think it was a brilliant idea. I honestly do…. I am no computer wizard believe me, I am a one finger typist and I probably made a few mistakes but for me to understand it had to be simple and it was. Well I don't think you could make it any simpler can you. Like once I posted those results on there, they went straight to the doctor and evidently you received them. See that was all I had to do, just wait and she sent me back the dosage for the following week... it was simple. Really good. I don't think it could get any better. (Craig)*

> *…it was just great I'd just log on and it shows you what the last thing was and then he could send me an email or ring up and say stay on the dosage you are on now, it was brilliant… (Jack)*

Participants also appreciated the ability to transmit results to their GP without having to interrupt the workflow of the GP and having the ability to have the GP send through their dosing advice at their convenience:

> *…the easy communication, you know I am not disturbing the doctor and you know she'd just review it at the end of the day and her receptionist would pop it on the computer… (Sally)*

> *…once me and [the GP] had it right, It meant that, I wasn't telling him every INR I did, I sort of was telling him once every couple of week, what the INR was, but this way, he could go back and even if I didn't do the notification that I had put up an INR he could go back and see that it was stable anyway, and yeah it worked really well. (Gabby)*

There were mixed responses regarding the use of the site whilst travelling. Sally travelled interstate on holidays and reported a positive experience, "I went away and I could do it all and I could still get online and put in the results and yeah, so it is much easier than trying to find a Pathologist or yeah, no it is good", while Wendy headed away on a long overseas holiday and described a less positive experience:

> *The [website] itself didn't work altogether well whilst I was in Europe on a Wifi situation because the wireless interconnection were too iffy and as a result of that, it was fairly frustrating. (Wendy)*

Other problems with the website related to the computer literacy of the patients or GPs and the execution of the web design and layout. A number of GPs contacted the project team for additional assistance during the trial, while others like Sally's GP sought assistance from practice staff "she is not the most computer literate doctor out of all of them, but her receptionist does it all and [the GP] just reports and [the receptionist] puts it in" (Sally). Paul was one patient who had particular issues using the website, however did not contact the project team during the trial to seek assistance or further training:

> *I don't get along well with my computer at all, and I have to be quite honest with you, you know I am just too old and I struggle along with it, but I get extremely confused very easily, just frustrated because I don't know how to fix the problem that is facing me on the screen, this is, you know, I am not a natural in other words. I found the layout of the computer program was just absolute nonsense,*

> *it could have been so simple, but they made it so difficult, you know, it just needed to be plain, what you looking at on the screen just plain and quite obvious what the next step is, by pointing arrow to do this or do that. I just found it very confusing. I mean it is probably no more complicated than most websites, but there is no reason for it to be as complicated as it was, that is all. (Paul)*

Robyn experienced similar issues with the functioning of the site but, in contrast to Paul, was an experienced and competent computer user, suggesting the website may have posed usability issues for people of all computer literacy levels:

> *The website is pretty dodgy… It's a good concept, but whoever is setting up, I don't think they go in there enough to fix it enough. But it is not too bad and I think the idea of it is quite good. You just need someone who is quite on the ball with programming it. (Robyn)*

Overall, the qualitative feedback suggests that the web-based platform concept was one which appealed to this group of self-monitoring patients. However, there were some issues with the execution of the design which resulted in usability issues for some patients. Future iterations are likely to benefit from usability testing in a wide range of people of various levels of experience with the internet to identify specific aspects of the design which could be altered to improve the experience of users.

4.4 Discussion

Since its launch, www.anticoagulation.com.au has received strong support from the Australian healthcare industry and consumer bodies. Links to the site appeared on the National Stroke Foundation website, in the Melbourne Pathology 'Warfarin Care Patient Guide' booklet and in the '50 something' magazine produced by National Seniors Australia. Additionally, the manufacturer of both brands of warfarin available in Australia, Sigma Pharmaceuticals (now Aspen Pharmaceuticals), included www.anticoagulation.com.au in their booklet 'Warfarin: Important Instructions for Patients'.[358] This booklet is a resource distributed by the company to pharmacies and hospitals throughout Australia for use when providing information to all patients, particularly those newly commenced, on warfarin.

The high utilisation rate of the www.anticoagulation.com.au website supports the existence of significant interest in the topic of anticoagulation and the previously identified lack of reliable online warfarin information. It also supports the potential importance of the site as a credible online resource for health professionals, patients and carers not only within Australia, but around the world. Many of the users of the site were return users, indicating that those who found the site were likely to find it useful enough to return to in the future for further information.

The relatively low utilisation of the self-monitoring resources is likely to be attributable to a number of reasons. Firstly, the resource was promoted as an anticoagulation resource for all patients and healthcare professionals looking for information on warfarin. Secondly, the resource was promoted and primarily used within Australia where self-monitoring is not yet a common management strategy. As few people are currently even aware the option is available, it is not surprising that these resources received low levels of utilisation.

One of the strengths of this site was its ability to evolve in response to feedback received from users and stakeholder organisations. Undertaking an iterative design process and considering issues of usability, accessibility and readability enabled the development of a website which appears to have been well received and highly regarded by patients, health professionals and the pharmaceutical industry. This evolution process resulted in a recent Australian study finding www.anticoagulation.com.au to be the top-ranking warfarin-related website on the internet in terms of quality, suitability and readability.[359]

The impact of the initial promotion on visit numbers was prominent and supports the adoption of strategies for ongoing promotion in the future. Studies in other areas have demonstrated that providing health professionals with prompts increases the likelihood that they will record information or provide a patient with information.[360] Providing ongoing education and reminders to health professionals about the existence of this resource would likely ensure they continue promoting it to their patients and using it within their practice.

As downloadable resources were provided in a portable document format that enabled users to save copies of the resources, we were unable to accurately estimate the extent of their distribution. Anecdotally, a number of pharmacists use the resources as counselling tools in their practice. They need only have downloaded the materials once to enable their continued use. The number of resources distributed from www.anticoagulation.com.au is predicted to be much greater than the number of downloads observed.

4.4.1 Limitations

One of the limitations with the data that were collected on the use of this website was the inability to distinguish between patient and health professional visits. A number of methods for achieving this were discussed but an ideal solution was not

identified. A survey embedded within the site elicited some useful comments which enabled changes to be made to the site in response to user feedback, but the uptake of the questionnaire was not sufficiently high to make assumptions about the volume of visits from either group.

The statistics package capturing data on the use of the site lacked the detail to list the number of views per page, meaning an exploration of which aspects of the information users were most interested in was unable to be performed. An exploration of the order in which people navigated through the site to identify what topics drew people's interest and any potentially uninteresting areas through common exit points was also unable to be performed.

An additional limitation to this study is the limited number of formal analyses which were undertaken on the website resource. Ideally, formal usability testing and focus group-type feedback would have been sort from a range of end users of the website to evaluate it from both a content and functionality perspective. Logistical and time restraints prevented further analyses of the site from being undertaken.

4.4.2 Future directions

This website has changed and evolved in response to user feedback. While the site has been favourably compared to other online resources providing anticoagulation information, there are many opportunities for future development. The potential exists not only to improve the comprehensiveness of the information included, but also to add further functionality. Potential plans exist to incorporate updates for health professionals on new anticoagulant developments, forums for people to discuss their treatment with other users, decision support tools for prescribers, targeted educational interventions for registered patients of the site, and online education modules for health professionals. Other suggestions have included the addition of resources in languages other than English, including pictorial counselling

tools, and large print resources to increase the range of patient groups who may benefit from the site.

The goal is for www.anticoagulation.com.au to firmly secure its place as the leading online anticoagulation resource, and to evolve into one part of a broader suite of sites representing a comprehensive online platform of resources for a range of chronic disease states.

4.4.3 Conclusion

www.anticoagulation.com.au has proved to be an important educational resource for both patients and health professionals. It continues to evolve to the needs of users and to be a popular, quality source of anticoagulation information for people across the world. The online INR monitoring platform was a popular concept that, with some further modifications, could prove to be an extremely valuable tool for patients and their healthcare providers in improving the convenience of monitoring warfarin therapy as part of a self-monitoring model.

Chapter 5 : Development and Implementation of a Flexible Anticoagulation Monitoring Service for Community Pharmacies

5.1 Purpose of the study

Anticoagulation management occurs in a number of clinical settings, including in specialised anticoagulation clinics. Clinics are generally regarded as offering benefits over office-based models of care as they tend to be more systematic in their approach to testing and follow-up and incorporate ongoing patient education.[12] They have also been shown to improve INR control when compared to patients managed in office-based settings.[56] The role for pharmacists in the community to conduct anticoagulation clinics and improve timely access to INR monitoring has been successfully demonstrated in a number of countries.[208, 331, 333-337] Pharmacists also have important roles to play in improving access to reliable warfarin education and facilitating PSM.

The aim of this project was to assist in improving anticoagulation management in Australia. The project aimed to address the individuality of community pharmacy practice, and address any barriers to effective anticoagulation management by:

- Developing an implementation toolkit to enable the implementation of pharmacist-delivered anticoagulation services through community pharmacy;
- Evaluating the toolkit contents in a community pharmacy setting; and
- Exploring the barriers and facilitators of implementing a flexible model of pharmacist-delivered anticoagulation monitoring services through community pharmacy.

5.1.1 Context

This study comprised two separate projects. The first enabled the development of the tools and an initial evaluation in a pilot involving three rural community pharmacists. The author designed the pilot study and wrote the grant application for this project. The feedback from the pilot study enabled the refinement of the resources and their subsequent use in a larger project involving pharmacists from both rural and metropolitan practices. The subsequent study design was essentially the same as the author used in the pilot study, on a larger scale. The author managed both projects from inception to completion, performing all recruitment, data collection and analysis.

5.2 Methods

This project was designed to develop training materials to equip pharmacists with the necessary training and support to provide quality anticoagulation services to their communities, and to trial the implementation of this training in a number of communities. It was designed to evaluate the feasibility of pharmacists to undertake self-directed training, and to implement an anticoagulation service with limited assistance from researchers. The project aimed to simulate a real-world situation where pharmacists would be provided with information, resources and telephone support, but not necessarily have the benefits of a face to face facilitator for the service. This required the development of a number of remote-delivery resources, recruitment of pharmacists, and for the pharmacists to then utilise these resources to implement a service. An evaluation process was included to assess the suitability of the developed resources, and the success of service implementation.

Community pharmacists were provided with a suite of resources to enable them to implement a range of potential services, including in-pharmacy POC monitoring, facilitation of PSM, and remote POC monitoring, for example as part of an HMR. These resources were underpinned by information available on www.anticoagulation.com.au. The participants were asked to individualise the service they implemented based on their pharmacy, local community, professional desires and experience.

This project was conducted in two phases - a small pilot study in three rural pharmacies, and a larger follow-up study in pharmacies from any state or region.

Following the conclusion of this study the author had the opportunity to travel to New Zealand to visit the innovative pharmacy practice which formed the starting point for the New Zealand pilot into pharmacist-delivered anticoagulation services. While this visit did not assist in the implementation of the service in this study, it did

give an interesting perspective on other factors which may facilitate the implementation of such services.

5.2.1 Pilot study

5.2.1.1 Development of resources

This project involved the development of resources to train pharmacists in anticoagulation monitoring services. Some of these resources had already been developed for use in the Pharmacy-Based Model Enabling Patient Self-Monitoring of Warfarin: Development and Evaluation project described in Part Three of this thesis. The existing resources that were used in this project were:

- A train the trainer package to train accredited pharmacists to enable patients to self-monitor their warfarin therapy (Appendix 15). This was converted to a resource that was capable of being delivered as DVD modules, with telephone support provided where necessary; and
- A train the patient package for accredited pharmacists to use to train patients to self-monitor (Appendix 16).

Additional resources and development that were required for this project were:

- Standard operating procedures to assist pharmacists to provide safe and professional pharmacy-based INR monitoring services; and
- Pharmacy business models to assist pharmacists to provide sustainable services. Business models were developed for all aspects of the anticoagulation monitoring services, including providing pharmacy-based INR monitoring, and providing training for PSM to patients. These models included strategies to assist pharmacists to liaise with other healthcare

professionals to ensure a multi-disciplinary decision on which model best suits their community.

The business models, liaison strategies, standard operating procedures and templates were incorporated into an *Implementation Toolkit for Point of Care INR Monitoring Services in Community Pharmacies* (Appendix 17). This document will be referred to as 'the Implementation Toolkit' or simply 'the Toolkit'.

5.2.1.1.1 Development of the Implementation Toolkit

A literature review was undertaken to identify and evaluate published studies relating to the implementation of services, primarily in a healthcare setting, to enable the informed development of the Implementation Toolkit. The Toolkit was developed to clarify common standards for the provision of anticoagulation monitoring services in primary care, and to provide the necessary tools and skills for implementation of a safe, effective and sustainable service in community pharmacies.

The author had previously been trained in systematic review and meta-analysis methodology and used a broad-ranging literature search strategy to identify relevant papers. Search terms related to the four major themes of 'decision making, 'liaison strategies', 'implementation guidelines for POC services' and 'development of community pharmacy services'. Searches were limited to human trials published in English between 1990 and 2008. The Medline, EMBASE, Cochrane Library, Google Scholar and the Medline 'Related Articles' function were utilised, while hand searching of Citation Search, conference proceedings, key individual journals, government documents, the AusPharmList website and references of excluded reviews was performed.

The information identified during the literature search was supplemented with reviewing suggested procedure templates for the provision of similar services in

pharmacy environments (such as the Quality Care Pharmacy Program procedure template for blood glucose testing), information on costs of consumables and discussions with pharmacists who have experience in offering similar services in their pharmacy. Also of value were discussions with a pharmacist who had participated in a previous project of pharmacist-delivered INR testing in rural community pharmacies[335] who had continued to provide an anticoagulation service for many years after the conclusion of the study.

The Toolkit was broken up into five sections: point of care INR theory, liaison strategies, business models, standard operating procedures, and templates (Table 15).

Table 15: Toolkit components

Point of Care INR Theory	This section provided pharmacists with background information on INR measurement and POC INR testing. It covered the accuracy of POC devices, and the rationale behind PSM.
Liaison Strategies	These strategies aimed to equip pharmacists with some of the resources necessary to liaise with local stakeholders regarding the proposed anticoagulation service. They encouraged pharmacists to engage in a multidisciplinary decision making process to ensure the service offered by the pharmacy would be supported by the community and was likely to be successful and sustainable.
Business Models	These models aimed to give indicative costs of providing each service and to make suggestions of possible models of remuneration for offering each service.
Standard Operating Procedures	These were intended to be comprehensive and cover all areas of the testing process for each service. They were detailed in order to ensure POC INR testing would be conducted safely and professionally by the user.
Toolkit	This section consisted of templates for the pharmacists to use at each step of the implementation process. They ranged from letters to GPs introducing the service and promotional flyers, to INR result forms and quality control records. An additional template, an advertorial for the local newspaper, was added during the pilot study following a participant request.

The Project Advisory Group was consulted in the development of these resources, and particularly in the development of the standard operating procedures. The Project Advisory Group was enlisted to review materials developed for the Toolkit project and had extensive input into the content of the standard operating procedures and the pharmacy business models.

During the development phase the author had the opportunity to conduct training in POC INR testing for a rural GP wanting to use this model of management in their practice, and for the peri-operative nurses of the Royal Hobart Hospital who were moving towards using POC INR testing in their pre-op clinics. The author also had email contact with a pharmacist-run anticoagulation clinic in Singapore. These opportunities informed the development of the tools and assisted with highlighting which aspects of the Toolkit, in particular aspects of the standard operating procedures, would be of most importance and what key points must be included in this document.

5.2.1.2 Recruitment of pharmacists (Pilot)

Pharmacists were recruited to participate in the pilot project through advertisements placed in three pharmacy publications: the Australian Pharmacist, AusPharmList, and Pharmacy Daily. The advertisements were published in March and April 2009 and invited interested rural and remote pharmacists to contact the research team to register their interest in participating. An example of these advertisements can be found in Appendix 18. The first three interested and eligible pharmacists that responded to the advertisements were recruited to participate.

5.2.1.3 Pilot of Implementation Toolkit (Pilot)

Pharmacists were provided with a number of tools to assist them to implement an anticoagulation service in their community pharmacy. The tools and resources they were provided with included:

- The train the trainer manual (Appendix 15), as well as an accompanying DVD module of presentations and a CD of supporting background materials. This was provided to give the participating pharmacists a refresher in anticoagulation theory to prepare them for implementing an anticoagulation service. It could also be provided by the pharmacists to their local

accredited pharmacist(s) to up skill them to become competent in training patients for PSM;

- The train the patient manual (Appendix 16), for use if they had any patients interested in being trained to undertake PSM;
- The Implementation Toolkit (Appendix 17), containing liaison strategies, business models, standard operating procedures and a Toolkit of templates to assist in setting up and running an anticoagulation service. This was accompanied by a CD containing electronic versions of the templates and some additional references;
- A CoaguChek®XS device, CoaguChek®XS test strips, and single-use AccuChek® Safe-T Pro lancets. These were provided to facilitate the implementation of a service by the pharmacist;
- A hands-on training session with the CoaguChek®XS device was organised for each of the pharmacists and their staff. This was conducted by a representative from Roche Diagnostics Australia;
- Enrolment in the external Quality Assurance Program (QAP) run by the RCPA to ensure the CoaguChek®XS device used to conduct the service could be relied upon to provide accurate and reliable results; and
- Direction to www.anticoagulation.com.au to provide participants with patient-friendly resources and to enable them to improve their level of patient education.

The pilot implementation period was six months. In this time pharmacists were asked to liaise with local stakeholders and decide on an appropriate service to offer. They were then asked to make steps towards service implementation including staff

training, setting up equipment and infrastructure, promotion and recruitment. It was intended that the pharmacists would have implemented a service in this six month period. Pharmacists were telephoned and/or emailed approximately monthly throughout the intervention period by the research team. This contact was to provide pharmacists with support and encouragement where necessary. Participants were invited to contact the research team where necessary to resolve any issues related to the implementation of the service.

5.2.1.4 Evaluation process (Pilot)

5.2.1.4.1 Evaluation questionnaire

The participating community pharmacists were provided with an evaluation questionnaire exploring opinions of the Implementation Toolkit, the online resources and DVD training modules, and aspects of the business cases. The evaluation questionnaire can be seen in Appendix 19.

5.2.1.4.2 Stakeholder feedback

Stakeholder feedback was primarily sought by Ian DeBoos, as an external consultant to the pilot study. The methods and results presented here have been extracted from his report, although they have been extensively modified. As such, these findings are presented as study background rather than as part of the PhD research. The author was involved in the writing of the standard discussion guides, responsible for participant recruitment, and was involved in data validation and reviewing the original report.

The consultant interviewer was enlisted to conduct interviews with the pharmacist participants to evaluate the tools and resources. Telephone depth interviews were conducted with the participating pharmacists following the intervention period. The objectives of the stakeholder feedback were to:

- Determine the drivers of pharmacists' participation in the pilot study and more generally to gain an understanding of their interest in providing an anticoagulation service;
- Outline the process whereby decisions were made regarding which form of services to provide, including an identification of the key decision makers and decision influences;
- Ascertain the barriers to implementing the chosen anticoagulation service, including the respective roles played by pharmacists, patients and medical practitioners, including:
    - Patient response and barriers to adoption of the service;
    - Likely acceptance of the service;
    - Fit with current warfarin management practices (GP POC etc.); and
    - Likely fit with current pharmacy operations.
- Evaluate the effectiveness of the Implementation Toolkit for use by rural/remote pharmacists including:
    - Ease of use and comprehension;
    - Estimated ease of service implementation using the Toolkit;
    - Usefulness of the components;
    - Utility of the 'liaison strategies', 'business models' and 'standard operating procedures' sections;
    - Level of confidence in using the Toolkit; and

- Suggested modifications to the Toolkit, suggested additional or redundant components.

The three pharmacists who had enrolled in the trial of the anticoagulation service and who had received the Implementation Toolkit formed the sample.

These people were contacted by telephone and recruited to participate in telephone depth interviews at a time convenient to them. Remuneration was provided to the respondents for their time taken to participate in the interviews.

A topic guide (Table 16) covering the key issues was developed in association with the research team. This instrument was then used to direct the interviews. All interviews were audio taped with the respondents' permission and subsequently were transcribed verbatim.

Table 16: Topic guide for stakeholder interviews

Background	What is the 'usual' process for managing anticoagulated patients in your community.
Positive experiences	What aspects of the new anticoagulation management service you are providing do you consider to be effective/successful?
Facilitators	What factors or processes contribute to you providing high quality care of patients in your community on warfarin?
Negative experiences	In your experience, what problems do patients face while being managed on warfarin?
Barriers	What factors or processes prevent patients on warfarin receiving the best possible care in your community?
Overall outcomes	Overall, how would you describe your experiences of managing patients on warfarin through your new service?
Possible personal contribution	Do you see any ways that you, as a pharmacist, could improve the experience of patients on warfarin?
Willingness to contribute to care	Would you be willing to become more involved in managing warfarin therapy in your community? E.g. through implementing a service similar to those outlined in your resource kit
Other contributions	Do you have any other suggestions as to possible processes or services that may improve the care of patients on warfarin in your community?

Analysis comprised multiple readings of the transcripts to identify apparent themes, similarities and differences in responses; quotes were extracted to illustrate findings.

5.2.1.5 Handling of data (Pilot)

All data was treated confidentially and anonymously. The names of participating pharmacists were not stored with questionnaires or data files on computer.

5.2.1.6 Ethical approval (Pilot)

This pilot project received ethical approval from the Human Research Ethics Committee (Tasmania) Network (H10428).

In addition to ethical approval, advice was also sought from Pharmaceutical Defence Limited, the company which provides professional indemnity cover to 95% of Australia's pharmacists, as to whether this was an activity that would be covered under a standard policy. They felt, provided the pharmacist had undertaken appropriate training, such as that provided in this study, this activity was within the scope of practice of a pharmacist and would be covered. Their response can be seen in Appendix 20.

5.2.2 Follow-up study

5.2.2.1 Refinement of the Implementation Toolkit (Follow-up)

The Toolkit was refined for use in this follow-up study based on the feedback from the rural and remote pharmacists who participated in the pilot study. Very few suggestions for changes were made by pilot study participants. To address the feedback from the pilot study participants, one further material was included in the Toolkit template section; an advertorial for newspaper advertising. The contents of the Toolkit was also generalised to remove the focus on rural and remote practice, to make it more widely applicable to all community pharmacy practice.

5.2.2.2 Recruitment of pharmacists (Follow-up)

Pharmacists were recruited to participate in this follow-up project through a number of means. Pharmacists that applied to participate in the rural pilot but were ineligible on the grounds of location were approached via email to participate if they were still interested. At the Pharmacy Australia Congress in Sydney in 2009 a number of pharmacists completed questionnaires on pharmacist-delivered INR testing. A number of these expressed an interest in participating in future projects and were subsequently invited to participate. The third means of recruitment was through PSA practice support officers. PSA's Pharmacy Support Program is a consultancy service offered to pharmacists and field officers provide in-pharmacy

support for the implementation and delivery of professional services, as well as other elements of practice change. One practice support officer who had been familiar with the rural pilot project contacted the project team to discuss the possibility of offering INR testing as one of the professional services she could assist pharmacists to deliver. This lead to a number of other practice support officers also wanting to offer this service and subsequently recruiting pharmacists to participate in the project on our behalf.

5.2.2.3 Implementation of an INR service (Follow-up)

As in the pilot study, pharmacists were provided with a number of tools to assist them to implement an anticoagulation service in their community. Pharmacists were encouraged to use the tools and resources provided and to implement the service most appropriate and sustainable for their community. The key differences in the resources provided between the projects is shown in Table 17:

Table 17: Resources provided in pilot and follow-up studies

	Rural and remote pilot study	**Follow-up study**
CoaguChek®XS device	✓	✓ *(on loan)*
CoaguChek®XS test strips	✓	✓
AccuChek® Safe-T Pro lancets	✓	✓ *(sample)*
Hands on training from Roche Diagnostics Australia	✓	✓
Enrolment in the RCPA QAP	✓	✗
Visits from PSA practice support officers	✗	✓ *(some but not all)*

As with the pilot study, the implementation period for the follow-up study was six months. In this time pharmacists were asked to liaise with local stakeholders and decide on an appropriate service to offer. They were then asked to make steps towards service implementation including staff training, setting up equipment and

infrastructure, promotion and recruitment. It was intended that the pharmacists would have implemented a service in this six month period. Pharmacists were telephoned and/or emailed approximately monthly throughout the intervention period by the research team. This contact was to provide pharmacists with support and encouragement where necessary. Participants were also invited to contact the research team where necessary to resolve any issues related to the implementation of the service. Some pharmacists also received face to face visits from practice support officers to assist them to implement professional services within their practice.

5.2.2.4 Evaluation process (Follow-up)

5.2.2.4.1 Evaluation questionnaire

Participating pharmacists completed an evaluation questionnaire at the conclusion of the implementation period. The questionnaire comprised both quantitative and qualitative data collection methods, exploring opinions of the Implementation Toolkit, the online resources and DVD training modules, and aspects of the business cases (Appendix 21).

Differences in rurality and socioeconomic status of pharmacy site were compared to identify any differences in responses which may have been attributable to location. The low number of responses failed to permit the use of parametric statistics, hence non-parametric statistics were utilised with medians and ranges, and Kruskal-Wallis test reported for comparisons. A p value of <0.05 was specified as statistically significant for all analyses.

5.2.2.4.2 Qualitative analysis

The qualitative evaluation sought to explore:

- Pharmacists' motivation for participation in the study and for providing an anticoagulation service;
- Decision making processes utilised;
- Barriers and facilitators to service implementation;
- Views on the Implementation Toolkit;

The evaluation was designed as explorative component of the research project and open-ended questions are a method of enabling participants to explain their experiences in their own words and prioritise the experiences which had the largest impact on their practice.[361] As such, a large portion of the evaluation questionnaire was comprised of open-ended qualitative questions.

A thematic analysis approach was adopted to analyse the participant's responses. Thematic analysis is one of the most commonly used methods in qualitative analysis,[362] and is a widely used approach in the analysis of open-ended questions of a questionnaire.[363, 364]

In thematic analysis the task of the researcher is to identify a limited number of themes which adequately reflect their data.[362] It is an iterative process, comprising a number of stages of analysis.[362] It is primarily an inductive process where points of interest are identified within the data rather than being guided by pre-established ideas.[361] The data is generally coded into categories to reflect increasingly broader perspectives.[361] At every stage of the analysis, the codes may be altered and modified as ideas develop.[362] Eventually, recurring issues may be grouped together to describe themes that emerge from the data.[361]

Analysis of the evaluation questionnaire comprised multiple readings of the responses to identify apparent themes, similarities and differences in responses; quotes were extracted to illustrate findings.

Differences in rurality and socioeconomic status of pharmacy site were compared to identify any differences which may have been attributable to location.

5.2.2.5 Handling of data (Follow-up)

All data was treated confidentially and anonymously. The names of participating pharmacists were not stored with questionnaires or data files on computer.

5.2.2.6 Ethical approval (Follow-up)

This follow-up project received ethical approval from the Human Research Ethics Committee (Tasmania) Network (H10992).

5.3 Results

5.3.1 Pilot study

5.3.1.1 Participants (Pilot)

The first three eligible pharmacists who responded to promotional materials were recruited to participate in this pilot project. Eligibility was determined primarily on the location of the pharmacy and being rural or remote. Remoteness of pharmacies in Australia is defined using the Pharmacy Accessibility/Remoteness Index of Australia (PhARIA) which measures the professional isolation of a pharmacy. A definition of rural or remote relies on the location being in an area categorised as PhARIA greater than 1. The participating pharmacists practiced at pharmacies that were located in rural areas of Queensland, the Northern Territory, and New South Wales. The demographic information of participating pharmacists is shown in Table 18 and their approximate locations can be seen in Figure 24.

Table 18: Pharmacy demographic information

Pharmacist	**1**	**2**	**3**
State	QLD	NT	NSW
PhARIA	4	3	3
Town Population	1200 + holiday makers	2500	15000
# GP Practices in town	1 (started during the pilot)	2	3
# GPs in town	1 FTE	6 FTE	8 FTE
# pharmacies in town	1	1	2
# pharmacists in store	1.5 FTE	1 FTE	2 FTE, 1 graduate
Participating pharmacist's role	Partner/Accredited Pharmacist	Employee/Pharmacist in charge	Partner/Pharmacist in charge
Participating pharmacist's country of training	South Africa	UK	Australia
# years in profession	28 years (7 in Australia)	9 years	8 years
# patients on warfarin	12-15	10-20	50
Patient demographic	Mainly elderly concessional	50% concessional	Mainly concessional
Usual care model for INR testing	People travel 30 mins to larger centre to have INR done.	INR monitoring done either through GP or the hospital via venous sample.	Most have their INR tested at the local pathology laboratory or the GP via venous sample. One GP practice has a POC INR device.
Access to accredited pharmacist	One on staff	Has access to them, is also working through accreditation process	One on staff

Figure 24: Pharmacist locations

5.3.1.2 Pilot of Implementation Toolkit (Pilot)

Pharmacists were provided with the resources and tools described in the Methods section above. They were then offered telephone support and given the opportunity to request further assistance and resources as required. One request for further resources was received from one pharmacist for a template for an advertorial piece to run in the local newspaper. An example of an advertorial was supplied as requested and can be seen in Appendix 22.

Pharmacists were encouraged to use the tools and resources provided and to implement the service they felt was most appropriate and sustainable for their community. The level of service provision of each pharmacist at the six month conclusion of the intervention period is summarised below in Table 19.

Of the three pharmacists, one implemented a service; one took significant steps towards implementing a service; and the third was unable to implement a service during the intervention period. The pharmacist who succeeded in implementing a

service offered a pharmacist-delivered monitoring service to a total of four patients. Three of these patients were holidaymakers travelling through town; the fourth was a local who later moved from the area. The fourth patient was impressed with the testing procedure and purchased a monitor before moving and subsequently enabled the pharmacist to also offer the self-monitoring training service. This pharmacist intended on working in collaboration with the new doctors in their town to continue to offer a service. The second pharmacist made significant steps towards implementing a service and approached local doctors about offering the service, prepared promotional materials, and conducted staff training sessions so all staff are aware of the service and appropriate staff are trained in preparation for service provision. This pharmacist also participated in a number of other research projects in 2009 involving service provision and prioritised the implementation of these services as they had concrete deadlines to be met. This pharmacist intended on resuming their efforts to implement an anticoagulation service in 2010 when their other project commitments had finished. The third pharmacist was a single employee pharmacist who was completing additional studies by correspondence at the time of taking on the anticoagulation service project. They found it difficult to find time to complete the training requirements and preparations for service provision. This pharmacist left the original pharmacy practice toward the end of the intervention period so the future of this service is uncertain.

Long-term follow-up of the three participating pharmacists 18 months after the conclusion of the study found that the first pharmacist continues to do occasional testing for holiday makers passing through the town and did have a regular client who has since passed away. They also continue to promote self-monitoring during HMRs and have facilitated the uptake of PSM for a small number of patients. The second pharmacist did implement a service and has a regular client whose GP is out of town, but has generally met with resistance from local GPs as they prefer their

patients to utilise the GP practice service. The third pharmacist is in the process of establishing a new pharmacy and plans to offer INR testing in this pharmacy once it is up and running. The pharmacy where he was employed during the study did not continue to offer a service in his absence.

Table 19: Pharmacist service provision summary

Pharmacist*	**1**	**2**	**3**
Service chosen to implement	Pharmacy-based monitoring service	Pharmacy-based monitoring service	Pharmacy-based monitoring service
Implemented?	Yes	No	No
# patients recruited into service	4 – one local who moved away, 3 travelling through the town	N/A	1 patient received once-off testing
Additional anticoagulation services offered	Facilitated PSM training for a local who moved away	Nil	Nil
What progress was made towards implementing an anticoagulation service?	Service implemented (staff trained, equipment set up, some promotion done, patients tested)	Training commenced	Doctors approached Service promotion prepared Staff training
Facilitators that assisted in implementing a service?	Local need – absence of both a local GP and a local pathology service Pharmacists had time available to conduct service Promotion of service in local newsletter Patients positive to service New GPs open to collaboration commenced in town during intervention.	Good relationship with local GPs Patients positive to service	Good relationship with local GPs Promotion in local newspaper and flyers in store Patients positive to service
Barriers faced in implementing a service?	More promotion needed	Pharmacist studying and working alone, struggled with training and implementing Moved pharmacies towards the end of the study period	Many additional services being offered Patient-GP consent process GP offered POC INR testing at one practice
Plans to continue a service?	Yes	Unsure	Yes

* numbers as per Table 18

5.3.1.3 Evaluation process (Pilot)

5.3.1.3.1 Evaluation questionnaire

The three participating community pharmacists completed an evaluation questionnaire at the conclusion of the implementation period. A visual representation of their responses and a full set of their comments can be found in Appendix 19.

All participants rated the Toolkit as useful or very useful, and particularly liked the template section. They also found the costing models to be useful aspects of the business cases. There were no improvements suggested to any aspect of the Toolkit or resources as they were felt to be comprehensive. All participants had decided to start by implementing a pharmacist-delivered INR testing service, primarily to complement existing professional services offered through the pharmacy, but also to address a perceived need within their community. Respondents were divided regarding the impact of this service on their relationship with patients and local GPs; however, only one doctor had specifically expressed a desire to not be involved. This doctor's concerns were financial in origin; he did not want his patients involved, as he would not receive payment for a consultation, and would also not be paid to interpret the results and make the subsequent dosage changes for any INRs obtained through the pharmacist-run service.

Participants found the train the trainer modules informative, easy to use and appropriate to the service they wished to provide. There were no changes suggested to the modules. Participants also found the web-based resources provided on www.anticoagulation.com.au easy to use and a useful resource. They particularly liked the fact sheets and the ability to print the information for patients.

Participants did not rate their service provision at the conclusion of the intervention period as very successful, though they were optimistic that the service they were

offering would improve. The poor rating of their service provision was not felt to be a weakness in the Toolkit, but a combination of other pharmacist- and pharmacy-related factors, including over commitment of those involved. The Toolkit was rated by all participants as a valuable tool requiring little modification. It was suggested by some that they would aim to improve the service with the assistance of local GP involvement, further promotion of the service, and by dedicating more time to service implementation. Promotional methods used during the intervention period varied between pharmacists, and included verbal promotion, posters displayed within the pharmacy, and advertorials placed in local newspapers.

5.3.1.3.2 Stakeholder feedback

The main findings identified during the telephone depth interviews with pilot study participants were:

Pharmacist demographics:

- The pharmacists involved in this study practiced at pharmacies which were described as rural. All three participants raised the issue of access to medical practitioners in rural areas without prompting. Attracting and retaining GPs was described as difficult and meant that patients face problems trying to get appointments. Weather patterns and large distances exacerbated the problems accessing medical care for the Northern Territory site.

Pharmacist characteristics:

- Two of the three interviewed pharmacists were partners in the business, and two of the three had trained and worked overseas. All three shared a professional interest in expanding the role of pharmacists and perceived that

the provision of clinical services though community pharmacy was the way of the future.

Current warfarin management:

- The manner in which INR testing was undertaken varied between and within towns, depending on GP preferences and available facilities. At the beginning of the study, the main role of the included pharmacists in the management of warfarin therapy was the provision of advice to new patients, in addition to dispensing the medication.

Drivers of participation in the study:

- Professionalism: The interest these pharmacists had in expanding their role beyond dispensing translated into a desire for involvement in a range of activities. They were actively looking for opportunities to participate in clinical programs.

- Providing a competitive edge: One pharmacist specifically wanted to offer an anticoagulation service for business reasons. They felt the service represented an opportunity to differentiate their pharmacy practice by offering something new, with the potential to increase customer loyalty.

- Perceived need: Pharmacists did not expressly consider that patients had difficulties having INR tests performed, but believed that having monitoring available through the pharmacy would add a level of convenience and service accessibility.

- Benefits: Both patients and, to a lesser extent, GPs were considered to potentially benefit from the anticoagulation service. Benefits were expected through the ability to perform INR testing at any time on any day, the less

invasive means of testing, and the ability to have INR results immediately available.

Decision making process:

- Collaborative process: The decision to provide a service was made in conjunction with other pharmacists in the business. The Toolkit encouraged pharmacists to engage local stakeholders in the decision making process. Despite this, GPs and patients were not consulted, and were later informed of the intention to provide a service after the decision was made.
- Form of service: Pharmacy-based monitoring was the default service chosen because of the perceived low number of patients who were likely to be able to afford a machine and take up PSM. This service was also a good fit with the pharmacists' aim of expanded service provision through the pharmacy.

Barriers to implementation:

- Pharmacist-related barriers included:
    - Over commitment: The major reason for not starting a regular anticoagulation service within the pharmacy was over commitment to other programs, particularly other Fourth Community Pharmacy Agreement funded projects.
    - Potential under-delivery: One pharmacist felt that there was no point starting to offer the service until everything was in place.
    - Multistage process: Patients obtaining GP consent prior to participating in the service was seen as a delaying factor.
- Patient-related barriers included:

  - Minimal barriers were identified at this pre-implementation stage, and patients were described as "extremely positive". It was suggested that barriers may arise when patients were faced with having to pay for the service.

- Medical practitioner-related barriers included:
  - Owning a CoaguChek®XS and performing POC INR testing within the surgery was associated with less GP enthusiasm towards the service. Financial concerns relating to the lack of reimbursement for time associated with following up results also impacted on GPs' opinions of the proposed service.

Implementation Toolkit:

- Ease of use: Two pharmacists assessed the Toolkit as very easy to use. The solo pharmacist found the amount of reading onerous and suggested that it could be improved by staggering the amount of information delivered.
- Comprehension: The Toolkit was assessed as easy to understand and read.
- Usefulness of components:
  - Business models: One pharmacist found this section useful to provide guidance on what to charge for testing.
  - Reliability of the device: One pharmacist described this section as useful as it was felt that it was likely patients would be interested in this information.
  - Templates: These were judged to be particularly useful by one respondent.

  - Dietary information: One pharmacist rated this as very useful to provide to patients.

- Level of confidence with use: Pharmacists were confident that they would be able to implement the service using the Toolkit.

- Suggested modifications to the Toolkit: These included an example for an advertorial to promote the service (which was provided during the intervention and can be seen in Appendix 22), and improving the way the materials are organised and delivered to the pharmacist.

Suggested modifications to the project:

- The major suggestion for modifying the model of service provision was to provide assistance with implementation. It was felt that having someone who was familiar with the process and the procedures of implementing an anticoagulation service would be helpful, particularly to solo pharmacists who struggle with feeling isolated in the process and digesting the volume of information provided.

5.3.2 Follow-up study

5.3.2.1 Participants (Follow-up)

Seventy-eight pharmacists were approached to participate, 39 were those who had already had contact with the project team; another 39 were identified by PSA practice support officers. Of the 78 approached, 36 provided consent to participate and received the project materials. A summary of the demographics of the 36 participating pharmacists (based on the classifications at the time of the study) can be seen in Table 20. The demographics of the individual participating pharmacists are displayed in Appendix 23. All states and territories were represented, with the exception of the Northern Territory.

Table 20: Pharmacist demographic summary

State			PhARIA*			ASGC-RA**			SEIFA***		
	N	**%**		**N**	**%**		**N**	**%**		**N**	**%**
NSW	7	19.4	**1**	30	83.3	**RA1**	25	69.4	**1**	0	0.0
Vic	7	19.7	**2**	1	2.8	**RA2**	6	16.7	**2**	2	5.6
Tas	3	8.3	**3**	2	5.6	**RA3**	5	13.9	**3**	4	11.1
SA	1	2.7	**4**	1	2.8	**RA4**	0	0.0	**4**	1	2.8
WA	8	22.2	**5**	2	5.6	**RA5**	0	0.0	**5**	4	11.1
Qld	7	19.4	**6**	0	0.0				**6**	4	11.1
ACT	3	8.3							**7**	8	22.2
NT	0	0.0							**8**	4	11.1
									9	6	16.7
									10	3	8.3

**PhARIA (Pharmacy ARIA) is a composite index, which incorporates measurements of general remoteness, as represented by ARIA (Accessibility/Remoteness Index of Australia), with a professional isolation component represented by the road distance to the five closest pharmacies. Values range from 1 to 6, with increasing degrees of remoteness with increasing values.*

***ASGC-RA (Australian Standard Geographical Classification – Remoteness Area) is a geographic classification system that was developed by the Australian Bureau of Statistics (ABS), as a statistical geography structure which allows quantitative comparisons between 'city' and 'country' Australia. Values range from RA1 (Major cities of Australia) to RA5 (Very Remote Australia).*[349]

****SEIFA (Socio-Economic Indexes For Areas) is another product of the ABS, which measures and ranks areas according to socio-economic and positional disadvantage based on information derived from the five-yearly Census of Population and Housing. The SEIFA is the most widely used general measure of socio-economic status by area. Values range from 1 to 10, with low values representing areas of 'disadvantage', relative to other areas of Australia, while high values represent 'advantaged' areas.*

The impact of the degree of rurality and socioeconomic factors on responses to the questionnaire and perceptions of sustainability were explored. No significant differences were found between the responses of pharmacies when grouped according to rurality or socioeconomic status ($p>0.05$ for all responses across all groups).

5.3.2.2 Implementation Toolkit (Follow-up)

No requests for further resources were received by the research team. Some pharmacists modified the templates to suit the requirements of their pharmacy and others created additional resources such as flyers and advertising posters. Examples of these modified resources are provided in Appendix 24. A request was received for an online forum to be included on www.anticoagulation.com.au to enable pharmacists participating in the implementation project to discuss issues with one another. The forum was set up and promoted to participating pharmacists; however, this was not used during the implementation phase by the participating pharmacies (the forum can be seen in Appendix 14, page 404).

Twenty pharmacists reported having achieved some degree of service implementation during the intervention period. The level of service provision at the six month conclusion of the study was lower than expected, particularly given the large number of participating pharmacists and the additional support that was offered to them to assist with implementation.

The services implemented by participating pharmacists ranged from providing testing free of charge, or at cost recovery to a small number of patients, to one pharmacist who reported performing more INR tests at a sustainable charge within the pharmacy than any other professional service test that they offered. One pharmacist withdrew from the project at the commencement of the implementation phase following negative feedback and a lack of support from the local GPs. Seven

pharmacists reported being unable to attempt implementing a service on account of illness (n=2), pharmacy renovations (n=3), pharmacist coordinating the project leaving (n=1), and sale of the pharmacy (n=1). Reasons for wanting to implement an INR service and reasons for not achieving the intended level of service provision are discussed in further detail below.

Positive feedback on the Implementation Toolkit was received from the PSA practice support officers. The PSA Project Manager of Practice Support said:

> *The Field Officers were wondering today if they could show all their pharmacists the resource folder from your study? There are pharmacists who don't want to implement an anticoagulation service, but in general your tool kit is the best example we have found for setting up a professional service. I think they would like to be able to show the pharmacists the types of things they should be considering when implementing a service, like your checklist.*

5.3.2.3 Evaluation process (Follow-up)

5.3.2.3.1 Evaluation questionnaire

Completed questionnaires were received from 28 pharmacists. Responses to quantitative questions are summarised in Table 21 and visual analogue scales are displayed in Appendix 21. There were no significances found between the demographics of those pharmacists who did return their questionnaire and those who didn't in terms of SEIFA (p = 0.33) and PhARIA (p = 1.00).

Participants rated the Toolkit as useful (median score 7.5) and open ended answers suggested they particularly liked the template section. Open ended questions suggested they also found the business implementation tools, the educational sections, checklists and the standard operating procedures to be useful. A few participants suggested improvements to the Toolkit. These included providing an

'easy to use' guide or summary page at the beginning of the Toolkit to make the process more streamlined and the inclusion of more comprehensive promotional materials, including flyers and posters. One participant also suggested the inclusion of a dose adjustment module in the future if the scope of practice of pharmacists is expanded to allow them to be responsible for managing dose adjustments.

Table 21: Summary of responses to evaluation questionnaire

Statement	Median response (range)*
How useful did you find the implementation toolkit?	7.5 (2.5 – 10.0)
I feel the service(s) had a positive impact on my relationship with my patient(s)	7.5 (0.0 – 10.0)
I feel the service(s) had a positive impact on my relationship with my local GP(s)	5.0 (0.0 – 10.0)
I found the training modules informative.	7.5 (0.0 – 10.0)
The content of the training modules was appropriate to the service I wanted to provide.	7.5 (0.0 – 10.0)
I found the web site easy to use.	7.5 (2.5 – 10.0)
I found the web site a useful resource.	7.5 (2.5 – 10.0)
I see the service(s) I implemented as being sustainable.	5.0 (0.0 – 10.0)

** Where a response of 10 indicated 'strongly agree' or 'very useful' and a response of zero indicated 'strongly disagree' or 'not at all useful'*

All participants who commenced the implementation process had decided to start by implementing a pharmacy-based INR testing service, primarily to complement existing professional services offered by the pharmacy, but also to address a perceived need within their community. Respondents were divided regarding the impact of this service on their relationship with patients and local GPs (median scores of 7.5 and 5.0, respectively).

Participants found the train the trainer modules informative, easy to use and appropriate to the service they wished to provide (all receiving median scores of 7.5). There were only two changes suggested to the modules. One was to make them more streamlined, the other was to include information on difficult situations

and error messages. This information was already included in the Toolkit, so perhaps it needed to be expanded or easier to find.

Participants also found the web-based tools provided on www.anticoagulation.com.au easy to use and a useful resource (median scores of 7.5). Open ended responses suggested participants found particularly useful and valuable the warfarin ID cards and the fact sheets and leaflets. They also reported the ability to print information for patients was very convenient. Participants perceived the information on the site as easy to understand, comprehensive yet concise and up to date. The website was described as a good tool that was easy to navigate by many participants. Two participants had a little more trouble navigating the site and thought this was an aspect that could be improved. Another suggestion for improvement was the inclusion of more information on the use of POC INR devices.

Participants did not rate their service provision at the conclusion of the intervention period as very sustainable (median response 5.0), though open ended responses suggested that many were optimistic that the service they were offering would improve. The poor rating of their service provision was not felt to be a weakness in the Toolkit, but a combination of other pharmacist-related factors, including over commitment of those involved. These factors are discussed in more detail below.

5.3.2.3.2 Qualitative analysis

As described in the methods above, the codes identified during the analysis process were grouped into themes. Participants described a number of different barriers and facilitators to implementing a pharmacy-based INR monitoring service, which could be further discussed in terms of client-centred factors, GP-centred factors, and pharmacist-centred factors.

5.3.2.3.2.1 *Facilitators*

Facilitators to providing an INR service within the pharmacy included receiving positive feedback from potential clients of the service and the pharmacist having a strong desire to be seen as having a point of difference from competitor practices. Participants did not describe any GP-centred facilitators to implementing a service.

Client-centred facilitators

Pharmacists described the responses they had had from patients, for example "patients said it was a great idea" and "I am loving being involved in INR and all patients on warfarin think it's a great service." They also gave specific examples of the feedback they had had from patients accessing their service:

> *Convenient, saves making a doctor's appointment to find out what dose I should be taking.*
>
> *This is an extremely handy service when I don't have time to see my doctor. I should be getting my INR checked more frequently.*
>
> *The monthly blood test bruises me... I love the fact that I can prick my finger and not bare a bruise for the next two weeks.*

The pharmacists that described having had positive responses from patients were more likely to describe having successfully implemented a service. Factors which seemed to impact on patients' perceptions of the service were their willingness to pay and their perceptions of healthcare professionals' roles in warfarin management. These are discussed in more detail in barriers below.

Pharmacist-centred facilitators

Another facilitator to implementing a service was the desire to provide a point of difference for the pharmacy business. The majority of participants stated the major

reasons they wanted to implement a pharmacy-based INR service were that they wanted to provide more services and assistance to the community and to offer professional services. Comments included:

> *To provide more service to the community as so many people are on warfarin and it is "serious" they stay within the right zone, otherwise serious sequelae could event…*
>
> *As an opportunity to make a move towards some "fee for service" ideas for our pharmacy.*
>
> *We are a service oriented pharmacy providing a strong point of difference to the discount chemists, so having this extra service was a welcome addition.*
>
> *This has come at an appropriate time as we have been trying to implement more professional services in our pharmacy as the Guild and so many other industry observers continue to indicate that these will be important for the viability of community pharmacy in the future.*

Pharmacists that had a desire to provide the service for pharmacy-centred reasons, such as having a point of difference, were more likely to describe having made positive steps towards implementing a service than those whose desire related to more altruistic, community-centred reasons.

5.3.2.3.2.2 *Barriers*

Analysis of responses revealed a number of barriers to implementing pharmacy-based INR services. These barriers are summarised in Table 22 and include factors relating to the potential clients of the service, the local GPs, the pharmacy and the pharmacists themselves.

Table 22: Barriers to service implementation

Client-centred barriers	The cost involved in INR testing at the pharmacy when it is free (bulk-billed) through the GP/pathology Perceptions that the POC device is less accurate than pathology testing Satisfaction with their current model of warfarin management Perceptions that warfarin management is the domain of the GP and is not a role for pharmacists
GP-centred barriers	Perceptions that the POC device is less accurate than pathology testing Satisfaction with their current model of warfarin management for their patients Perceptions that warfarin management is the domain of the GP and is not a role for pharmacists Having a POC device available at their practice Not viewing the instant availability of INR results as useful to their warfarin management model
Pharmacist-centred barriers	Not undertaking a process of liaison to establish what models of warfarin management exist in the community and what needs exist The loss of key pharmacists from the pharmacy preventing the service from becoming established The pharmacy undergoing renovations preventing there being space available to conduct a service Competing pressures on pharmacist time, resulting in a lack of time to dedicate to implementing a service

Barriers presented by potential clients of the service included the cost of having the test performed in the pharmacy, perceptions of accuracy of the POC device, being satisfied with their current model of care, and perception of the role of pharmacists in warfarin management. These were similar to barriers presented by local GPs who also had concerns about the accuracy of the device, were satisfied with the care their patients' currently received and did not perceive there to be a role for pharmacists in warfarin management. GPs also raised other barriers, including having their own

POC devices in the surgery and not perceiving a benefit in using a pharmacist-delivered service for instantaneous results.

Many respondents described discussions they had had with potential clients regarding the cost of the service they were offering. Many respondents suggested there needs to be a subsidy from the government to make pharmacy-based INR testing and PSM viable management options for patients.

> *Most patients won't pay as they get it done for free at their surgery.*
>
> *From talking to patients, it seems that the biggest barrier to using the service was cost as people seemed hesitant to pay $10 for a service that was offered free by local pathology labs. This may not have been the only barrier however. I suspect that people may have been more willing to pay the fee if the service had become part of their regular routine. Actually getting people to at least start using the service was difficult though because most of our patients (even though they expressed an interest when questioned) already had an INR monitoring routine involving regular pathology lab visits.*
>
> *Quite a few people said "I can get it done for free from a GP".*
>
> *Patients were mostly not interested in utilising a service they would need to pay for, when a free option subsidised by the government is available from pathology.*
>
> *I had told you about the in-store survey I ran for my regular warfarin patients and got a 100% negative response for paying for tests.*

One pharmacist described cost not being a problem for the potential clients of their service as they were based at an inner city location: "Yes, people are willing to pay

for this service – no problem!" However, their service had not become sustainable by the time of evaluation due to other factors.

Patients' perception of the accuracy of the device was also raised as something which made potential clients hesitant to participate. Some respondents found that this barrier was something that could be overcome by exposing clients to the device. One pharmacist commented:

> *One lady was very sceptical on the accuracy because her Dr said that the meter we use is not good enough! BULLOCKS!! (I think they say that to protect their $40 Medicare visit) One lady I checked always had INR of 1.7-1.9 and one day when I decided to try it out on my meter she got 3.1. She said that has got to be wrong! On questioning she said she had increased her fish oil dose greatly and had ceased eating any greens for almost two weeks. I said that would most likely explain it. Still a bit doubtful I told her to go to the Dr to request an INR to thus check the accuracy. (I was hoping she could prove the meter was accurate) the next day she received the result and it was 2.9!! She is now convinced and I told her that is well within 10% variation which would be a normal variation from one scientific lab to another. So she is now convinced.*

Concerns surrounding the accuracy of the POC device were also raised by local GPs, though they were less easy to convince of the machine's accuracy.

> *They also suggested that the readings done off the machine given could not be taken as 100% unlike a pathology test. They would not like to alter patients' doses on the readings we would provide. I suppose this becomes a medico-legal question? (if so this may be a valid point)… If the doctors are not behind this service then I do not believe it is something that we will be able to roll out at our site.*

Patients' perceptions of potential inaccuracy seemed, in some instances, to stem from their GP, and were likely to be related to their perceptions of the role for pharmacists in warfarin management.

> *The fairly old demographic that we have here I think still sees these tests as the realm of the doctor and are reluctant to have it done at the pharmacy.*

> *Some customers have shown an interest but we are still finding it a bit difficult to break that "warfarin is the domain of the doctor" mentality.*

GPs were also seen to be opposed to having pharmacists involved in the management of warfarin.

> *…very difficult to see or speak to some Drs who are very 'anti-pharmacist involvement' which could undermine their "God" status (in their mind) or take away consults from their income.*

> *They think that the patient should not obtain their INR reading at the pharmacy, as they may then not return to the doctor but instead alter their own doses. They think it is not a good idea as most patients as mentioned above have co-morbidities and or dementia.*

The perception of pharmacists not having a role to play in warfarin management was further compounded by many patients of participating pharmacists being happy with their current model of warfarin management.

> *I feel that, while INR monitoring is certainly a service that would be fantastic to provide, the majority of clients in our area find the relationship between the GP, pathology and themselves very timely and seamless.*

> *We have approached all of our regular patients who are currently on warfarin (we are a small semi-rural pharmacy) and all of them are currently happy with*

> *how their service is being provided. I had one patient who initially expressed interest who currently pays to have her INR's monitored but once she realised that she could not get any refund from us from Medicare she decided to stick to her current service as they will refund some of her costs. As our patients were happy with their current model of service I did not feel that it was appropriate to upset their current routine.*

Pharmacists reported that local GPs had also expressed a satisfaction with their current models of warfarin management.

> *One surgery already has an INR machine and can test there, and others prefer for their patients to have it done at pathology.*

> *They also suggested that pathology can do a two hour turn around and that there is no real need for an immediate reading; furthermore they mentioned that they have a CoaguChek®XS machine and most doctors could obtain one if needed, although they prefer not to use them.*

These barriers impacted heavily on the success of the implementation efforts by the pharmacists.

These barriers did not exist for all pharmacists, however, and could have potentially been identified prior to implementing a service if the recommended liaison strategies had first been undertaken. Many pharmacists described their pre-implementation liaison as 'discussions among staff' or 'brainstorming', both processes which did not enable the views of other stakeholders to be obtained or considered. Pharmacists that undertook more comprehensive liaison at the beginning either found that the service was unlikely to be sustainable as it lacked the appropriate support or that their service was likely to be supported and subsequently implemented a successful service.

Respondents discussed other pharmacy- and pharmacist-related factors that impeded their ability to implement a service. The major pharmacy-related factors were the loss of key staff and major renovations which prevented an appropriate testing area from being established during the trial period. Respondents commonly discussed time as being the major pharmacist-related barrier to service implementation. Expressions such as "Time always seemed to be against us", "Timing was a problem with me" and "Time management – as pharmacist it is often difficult to make the time" were common amongst respondents.

5.4 Discussion

5.4.1 Feasibility of the Implementation Toolkit

5.4.1.1 Evaluation of the Toolkit resources

The Implementation Toolkit as a resource received very positive feedback in both the pilot and follow-up studies. Participants saw the Toolkit as a valued resource that could be relied upon to provide the majority of administrative and training requirements to start a pharmacist-delivered anticoagulation service. They felt confident using the business models as a guide to incorporating a service into their existing business structure. The standard operating procedures were highly rated as they were felt to be sufficient to ensure that pharmacists could provide a high and consistent level of service delivery, regardless of which trained staff member performed the testing. The templates section of the Toolkit was found to be comprehensive and easy to use, especially in terms of the ability to brand the templates to the individual pharmacy. Overall, satisfaction with the resources provided was high and few suggestions for modifications were made.

Suggestions for additions to the Toolkit that arose from the pilot study included what to expect in terms of the time required to complete training and to set up the service, a list of the necessary resources required by the pharmacist, and suggestions on how to manage the coordination of patient documentation with the GP. It was also suggested that it may be helpful to include suggestions regarding the order in which the training material needs to be read and to provide indications of essential versus background information for each stage of implementation. These were included prior to distribution of the Toolkit for the follow-up study.

Suggestions for additions to the Toolkit arising from the follow-up study included providing an 'easy to use' guide or summary page at the beginning of the Toolkit to make the process more streamlined and the inclusion of more comprehensive

promotional materials, including flyers and posters. One participant also suggested the inclusion of a dose adjustment module in the future if the scope of practice of pharmacists is expanded to allow them to be responsible for managing dose adjustments.

5.4.1.2 Implementation of an anticoagulation service

During the intervention most participating pharmacists made positive and significant steps towards implementing a service. While an ideal situation would have seen all pharmacists having implemented a service in this time, this project aimed to create a 'real world' implementation experience and allow pharmacists to work on their service in a manner appropriate to their situation. The project targeted interested pharmacists and gave them the tools, and some remote support, to decide on and implement a service suited to their community. The research team did not see its role as one of applying pressure on participating pharmacists to implement, but rather to provide advice and guidance where required. Pharmacists were provided with self-directed training tools and all the necessary materials to implement an anticoagulation service, but were not given an exact recipe on what to do when. It was felt that this approach was likely to result in a more sustainably implemented service.

A number of work-related barriers to implementation were identified by participants, not least of which was over commitment in terms of pharmacist time to other tasks, including other research projects, and a consequent inability to focus on getting the anticoagulation service implemented. It was suggested by participants that their service provision was likely to improve and grow in the months following the evaluation, as other pressures diminished and they were better able to focus on the implementation of the anticoagulation service.

Interestingly, one barrier identified by participants in the initial pilot project was a lack of support throughout the implementation process. During the intervention period of the pilot the project team offered participants remote support via email and telephone contact. The budget did not allow for face to face support, though this may have been a key inclusion to improve service implementation. Participants identified the inclusion of a practice facilitator, someone who can provide one-on-one, face to face assistance, as something which would have been likely to improve the success of service implementation. This is consistent with the findings of Roberts *et al*.[306] who identified external support or assistance as one of the facilitators to professional service implementation. In this context, the practice facilitator would be someone external to the pharmacy practice who is familiar with the implementation process. Their role would be to complement remote methods of support. It is envisaged that this person would visit the pharmacist and provide one-on-one assistance with the implementation process. Some pharmacists participating in the follow-up project benefited from face to face visits by PSA practice support officers who were familiar with the INR service and the resources provided to the pharmacists. However, there was no difference seen between the success of service implementation between pharmacists who received face to face visits and those who did not. It's possible that the utilisation of these field officers as the source of face to face contact was less than ideal, and the inclusion of a practice facilitator who is solely dedicated to the implementation of INR services may make this role more successful.

The Toolkit was created to provide the resources for pharmacists to implement services which address a need within the community and to complement existing services. It was not designed to create service duplication in communities. It was to be used in consultation with other local health professionals to implement services appropriate to the needs of the local area. Pharmacists participating in both the

pilot and follow-up projects did not generally report involving local stakeholders, including GPs, in their decision making process. The practice facilitator role could be one that encompasses increasing interdisciplinary communication, which has been identified as a facilitator of successful implementation.[306] They could facilitate a consultation session for all local stakeholders, and/or detail GPs on the proposed service, and assist pharmacists in addressing any concerns. Pharmacists reported that local GPs were generally supportive of the concept of a pharmacy-based INR service, particularly if their practice was not using POC INR monitoring, though the pharmacists who implemented a service often found that this in principle support did not necessarily translate into support in practice. Communication with GPs, and involving them in the decision making process, would seem to be essential to secure their collaboration or to clearly elucidate their opinions before implementing a service which subsequently may receive no support from local stakeholders.

Patients were very positive towards the proposed pharmacist-delivered service. Pharmacists felt that when patients were asked to pay for testing, a number would be likely to prefer to continue with their current testing method. However, the pharmacists had generally not formally consulted patients on this issue, and one pharmacist subsequently found that the patients using her service were more than happy to pay $10 per test. Again, it is important for the services to be designed and implemented in collaboration with local stakeholders, including patients, to ensure a successful service that has the support of the community.

The barriers to implementation that were raised by participants in these studies are consistent with those previously identified in the literature. Time pressures, lack of remuneration for the costs associated with service implementation and provision, and the impact on relationships with patients and local healthcare providers have been previously discussed.[300, 301, 306]

Pharmacist-delivered anticoagulation clinics overseas enjoy a much different structure to health service remuneration than is currently in place in Australia. In Australia at the time of the study, there were only two means of remuneration from Medicare available to pharmacists. The first is the remuneration associated with the dispensing and provision of prescription medications, which includes reimbursement for the cost of the item and a fee to remunerate the pharmacist time associated with supplying the item and necessary accompanying information and follow-up. The second is a payment for providing medication review services to patients in the community or in residential aged care facilities on referral from their GP. At the time of the study there were no remuneration structures in place in Australia that enabled the provision of funded professional pharmacist services. However, under the Fifth CPA some professional pharmacist services, such as the recording of clinical interventions, now attract remuneration. However, the funding provisions under the CPAs are tightly linked to specified programs within the Agreement, with little flexibility to tailor programs to the needs of the local community. While the move towards funded professional services is an important step in making professional services delivered by pharmacists sustainable in the future, more can be done to ensure pharmacists can deliver services appropriate to the community in which they practice.

Internationally there are a number of different remuneration structures in place that are more conducive to sustainable service provision. For example, in the UK community pharmacists are now being recognised by the government as a mainstream contributor to primary care and public health, and remuneration structures have changed to reflect this. Pharmacists may now undergo additional accreditation and elect to provide enhanced-level pharmaceutical services, including anticoagulation clinics.[365] These enhanced services are commissioned by the local Primary Care Trust and remunerated by the National Health Service.[365] They enable

pharmacists to provide readily accessible public health services to reduce the burden on tertiary care centres and, being externally remunerated, represent a sustainable model of pharmacist-delivered service provision. A similar model of remuneration in Australia would greatly improve the chance of success of pharmacist-delivered services in this country.

In New Zealand, a pilot study was conducted involving 15 pharmacists to assess the feasibility of implementing pharmacist-delivered anticoagulation clinics by all interested community pharmacists. It was found that time in range improved for 77% of enrolled patients and that the program prevented 2.4 haemorrhagic events per 100 patient years.[366] This pilot was funded by New Zealand Health and resulted from a single pharmacist pilot in the Waikato region.[337] This single pharmacist pilot was the result of an innovative pharmacy practitioner working closely with the manufacturers of the POC device and a haematologist, as well as the ability for funding to be obtained from the local District Health Board. This funding enabled the service to be set up in a seemingly sustainable manner, with little cost to the patient, and for results to be obtained to encourage further funding from higher level sources, such as the national government. Integral to the New Zealand model is a high quality GP-pharmacist relationship, one which perhaps needs fostering for many of the pharmacists participating in this study. The ongoing sustainability of these services, particularly as they are rolled out on a wider scale around New Zealand, will be an interesting area to observe.

The introduction of the Medicare Local model in the Australian healthcare system over the coming years will take us closer to the New Zealand model, and may enable sustainable pharmacist-delivered anticoagulation services to be implemented and funded on a local level, in regions where interest is high. This may translate to greater support federally in years to come.

Pharmacists in our studies who reported higher levels of implementation success tended to be those who had expressed the desire to implement a service to give their pharmacy a competitive edge. This is a motivator of practice change and professional service implementation that has been identified previously by Roberts *et al*.[306] The other motivators identified by Roberts *et al*. included desires for increasing professional satisfaction and providing healthcare to the public, yet these played a noticeably less significant role for pharmacists involved in the anticoagulation service studies.

5.4.2 Limitations of the study

The major limitations of these studies, in terms of collecting meaningful quantitative data on service implementation and the potential benefits to communities, were the number of participating pharmacists. The pilot study involved only three rural pharmacists, while the follow-up study involved only 36 pharmacists. As such, the views expressed by the participants cannot be taken as being representative of the views of all pharmacists within Australia. It also needs to be noted that the pharmacists enrolled in this project because they were motivated to enhance the professional services offered by their pharmacy and were involved in a number of other professional service projects. These pharmacists may be considered early innovators and it cannot be assumed that all pharmacists will share the same level of motivation.

It should also be noted that in studies such as this, with such a small sample of participants, the results are vulnerable to be influenced by the actions of one pharmacist. The pilot study recruited the first three interested and motivated pharmacists who responded to the advertisement. These pharmacists did not succeed with implementing a regular service in the intervention period, however had three other pharmacists been the first to respond, the results may have been

very different. Remembering that there are around 5000 pharmacies in Australia, the same principles apply to the follow-up study where the results may have been significantly different if a different group of pharmacists with different characteristics had been recruited.

Participant feedback suggested that one of the reasons they had not yet achieved regular service implementation was that no formal deadline had been set and so the anticoagulation service received a lower priority than other projects the pharmacist was participating in. The lack of a formal deadline was intended to provide pharmacists with a more 'real life' experience where they implemented the service at a time and pace that suited their individual pharmacy. In retrospect it would have been more beneficial from a research perspective to have applied a tighter deadline to service implementation to improve the range of feedback received.

Finally, there was a time lag between when the pharmacists received the Toolkit resources and when the evaluation took place. This delay was intended to allow time for service implementation to occur but may have impacted on participants' recollections of specifics of the Toolkit. However, at all times throughout the project the informal feedback offered by participants regarding the resources was very positive.

In addition to the limitations associated with the feedback provided by participating pharmacists, it should also be noted that there was an absence of feedback from GPs and consumers who utilised the implemented services. The original project design did include collecting data from consumers and GPs, however the low levels of service implementation prompted a decision to abandon the collection of this feedback as the volume would have been far smaller and less meaningful than originally envisaged.

5.4.3 Conclusion

With minor modification the tools and resources developed in this project could be used in the future to investigate the implementation of pharmacist-delivered anticoagulation services. This process would likely be assisted by the involvement of a dedicated practice facilitator to assist with liaison activities, professional service implementation and delivery, and a change in the remuneration structure for professional service delivery by pharmacists in Australia.

PART THREE: FACILITATING PATIENT SELF-MONITORING OF INR TESTING

This Part describes a mixed methods study that explores the outcomes of PSM of warfarin therapy. For the purposes of this study, PSM involved patients testing their INR and returning to their GP for advice on dose adjustment. Some GPs allowed their patients to self-adjust their dose, while others assumed full responsibility for the dose adjustments of their patients. This was a decision left to the individual practitioners.

A triangulation mixed methods design was used, a type of design in which different but complementary data is collected on the same topic. In this study, INR results, including time within the therapeutic range and frequency of testing, are used to test the theory that PSM will improve outcomes for people taking warfarin in Australia. Concurrent with this data collection, qualitative interviews explore the lived experiences and perceptions of people performing self-monitoring. Quantitative and qualitative data are collected together to draw on the strengths of both forms of research in describing the benefits of INR self-monitoring from both objective and subjective perspectives.

The quantitative and qualitative aspects of this study are presented as two separate sections in the chapters that follow: Pharmacist-Based Model Enabling Patient Self-Monitoring of Warfarin and Exploration of Patient Views of Self-Monitoring of Warfarin. This Part of the thesis will conclude with a discussion of the results of both data collection methods.

Chapter 6 : Facilitating Patient Self-Monitoring

6.1 Purpose of quantitative aspect

The primary aim of the quantitative aspect of the Pharmacist-Based Model Enabling Patient Self-Monitoring of Warfarin study was to develop, implement and evaluate a pharmacist-centred pathway to enable Australians who take warfarin to monitor their own therapy. To achieve this aim, a number of intermediate objectives were identified:

- Development of training packages to enable pharmacists to train patients and to enable them to self-monitor;
- Development and implementation of a model to enable implementation of PSM in collaboration with patients, other healthcare professionals, and industry representatives;
- Evaluation of the model to allow for refinement; and
- Investigation of the outcomes of PSM for patients.

The quantitative aspects of this project was designed by a larger project team comprising Luke Bereznicki, Gregory Peterson, and academics from collaborating universities prior to the author becoming involved. The author acted as project manager, recruiting participants, facilitating training, performing all data collection and analysis.

The quantitative sections present the results of this research, and their implications for the widespread implementation of PSM of warfarin therapy in Australia.

6.2 Purpose of the qualitative aspect

The aim of this part of the study was to employ qualitative methods to explore the experiences and perspectives of individuals undertaking PSM. Most studies examining patient perspectives of PSM have used surveys or other forms of quantitative methods. However, given the inherent complexity of the lived experiences of patients, it is likely that qualitative research methods could provide significant additional insight. A comprehensive literature search identified only one qualitative investigation of patient perspectives and experiences of PSM.

Throughout the initial phases of the quantitative research period it became clear that the impact of PSM on the lives of the participants could not be clearly illustrated simply using only the clinical data that was being collected. As such, the qualitative analysis is primarily concerned with the experiences of people undertaking INR self-monitoring and the different things that may impact on these experiences. The interest of this study lies in subjective descriptions of INR self-monitoring.

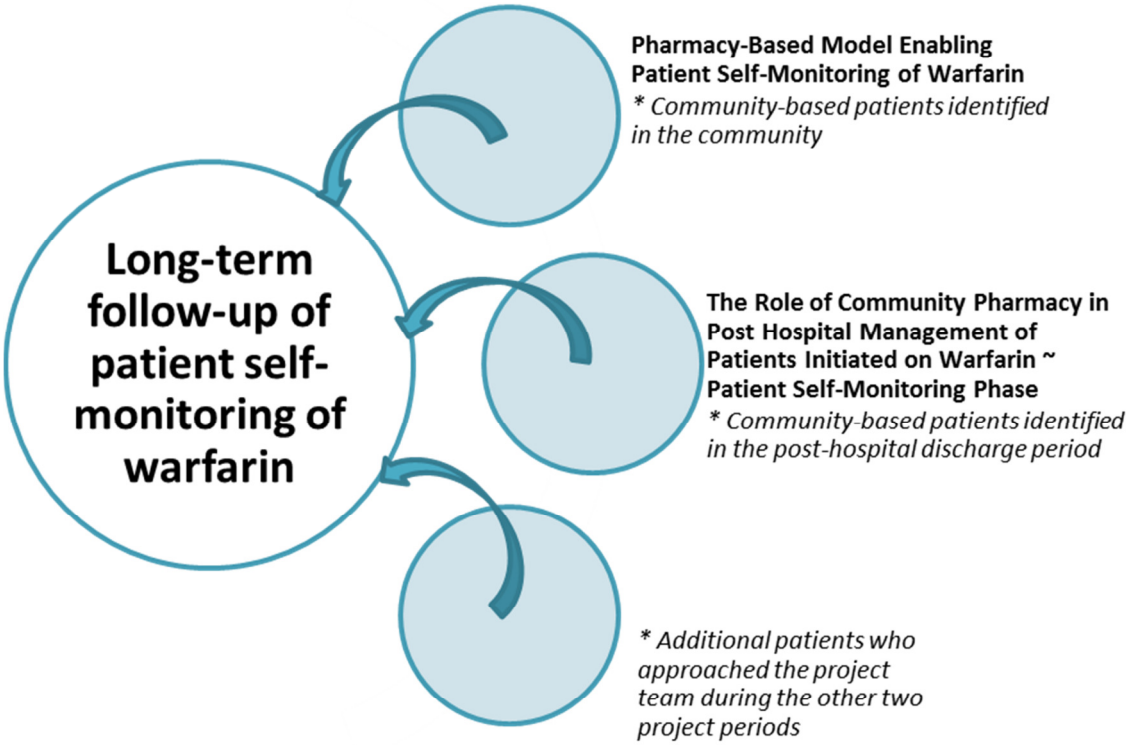
The qualitative aspect of this project was designed by the author, with input from Dr Emily Hansen. The author undertook all recruitment and data collection. Transcription was outsourced to a professional transcription service. The author performed all data analysis.

6.3 Methods

6.3.1 Pharmacist-Based Model Enabling Patient Self-Monitoring of Warfarin

The quantitative section of this chapter describes two distinct but similar projects involving patient self-monitoring of warfarin. Participants in these projects were then given the option to join a third project examining the longer-term outcomes for people undertaking self-monitoring (Figure 25).

Figure 25: Self-monitoring projects



The first project, Pharmacy-Based Model Enabling Patient Self-Monitoring of Warfarin, involved pharmacists identifying community-based patients taking warfarin and training them to undertake self-monitoring.

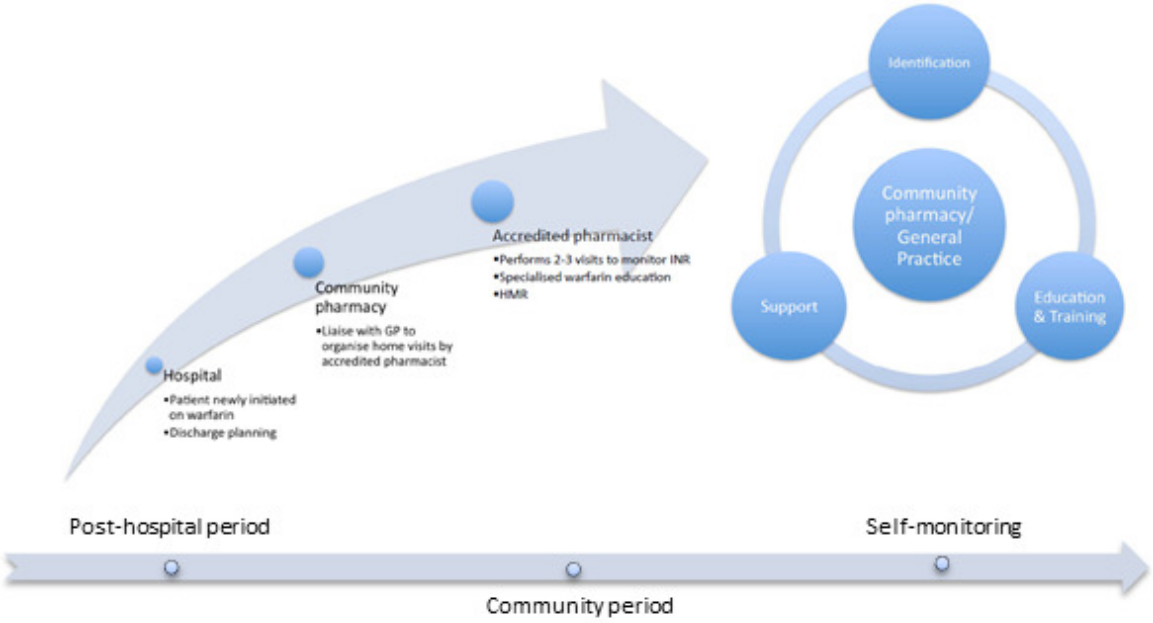
The second project was a sub-project of a study investigating the role of pharmacists in the post-discharge management of warfarin therapy, The Role of Community

Pharmacy in Post Hospital Management of Patients Initiated on Warfarin. The post-discharge aspect of this project forms the basis of the PhD thesis of Leanne Stafford. A number of patients who had been involved in the intervention phase of the post-hospital project were then invited to participate in the self-monitoring sub-study, referred to as the Patient Self-Monitoring Phase. The author was involved in project management, pharmacist and patient recruitment, pharmacist training and all patient support, data collection and analysis for the Patient Self-Monitoring Phase of this project.

The third project simply involved inviting participants of both of the previously described self-monitoring studies to continue to undertake self-monitoring for a longer period of time and was referred to as the Long-Term Follow-Up Phase. The design of the projects is very similar and as such the methods and results of these projects will generally be discussed together in the following chapters.

These projects, and the post-discharge aspect of the project mentioned above, fit together as part of an investigation into the involvement of pharmacists in enabling the smooth transition of anticoagulated patients from hospital to the community, including enhanced care within the community setting (Figure 26).

Figure 26: Transitional care model for warfarin management



6.3.1.1 Development of self-monitoring model

Members of the research team for this project, including the author, attended two different training courses at the University of Birmingham to assist in the development of a self-monitoring model suitable for the Australian healthcare environment. The course attended by other project team members was aimed at training patients to manage their own warfarin therapy, while the author completed the Masters in Oral Anticoagulation Management course, which focussed on training health professionals to use POC INR monitors and manage oral anticoagulation therapy. Both courses were valuable in the development of the final design and in the development of the educational materials discussed below.

6.3.1.2 Stakeholder consultation

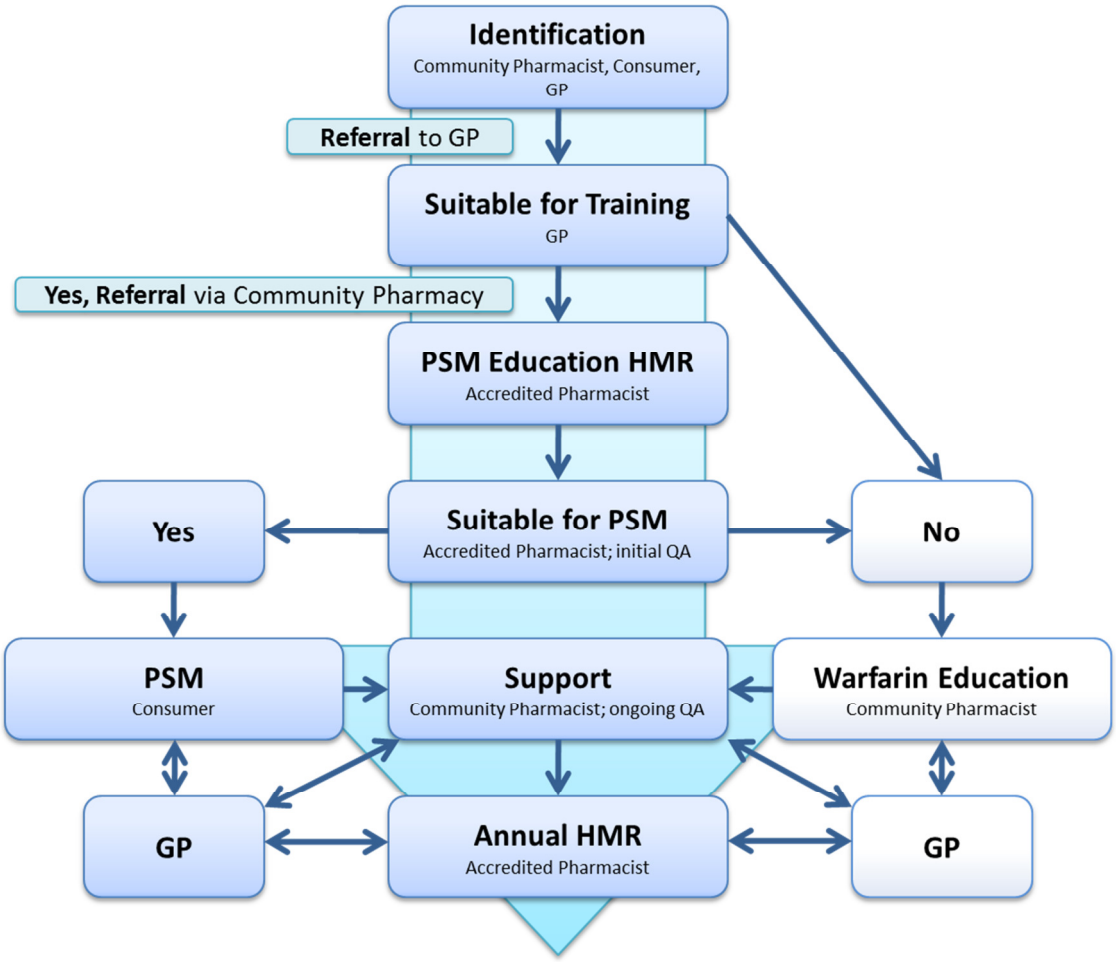
The Project Advisory Group had extensive input into the content of educational materials and the structure of the HMR used in the model. It was felt by this group that a quality assurance (QA) aspect was imperative to safely and successfully implement PSM in Australia. QA was included in the model in the form of two

comparison INR tests initially by patients on commencing PSM, and further comparison tests three to six monthly to ensure accuracy of self-obtained results. The comparison INR tests were to be performed within four hours of a venous sample being taken and had to be within 15% of one another to be considered acceptably accurate.[261]

6.3.1.3 Clinical pathway development

The final clinical pathway developed for this project utilised the existing HMR model and is shown in Figure 27. Community pharmacists were felt to be ideally placed to screen patients taking warfarin for their suitability to monitor their own therapy, and were recruited to identify suitable patients for this study. Under existing funding structures, pharmacists referred these patients to their GP to discuss the concept, with the view to their GP referring them to an HMR-accredited pharmacist for specialised PSM training, delivered as part of an HMR. As discussed earlier, the AACP accredits a specialised sub-group of Australian pharmacists to undertake HMRs for suitable patients. A number of these accredited pharmacists were up skilled using a train the trainer program, to teach suitable patients to monitor their own therapy using educational materials developed for this purpose.

Figure 27: Clinical pathway to enable self-monitoring of warfarin therapy



The HMR focussed on the provision of warfarin education but also included medication review and hands on training in the use of the CoaguChek®XS INR monitor. The education component of the HMR covered background on warfarin, risk of bleeding, diet, and the INR. The practical component covered a practical demonstration of using the monitor and other aspects, such as quality control and the storage and handling of test strips.

Once trained, a 'run-in' phase where patients completed two INR tests on the CoaguChek®XS in conjunction with two pathology tests to compare for accuracy ensured the research team, the GP, and the patient were satisfied that the monitor provided accurate results and could be used effectively. If the comparison tests

were not within 15% further instruction was provided. If further comparisons were subsequently not within 15%, the patient was excluded from the trial.

Once patients had been trained to perform PSM and had completed the 'run-in' phase, they were asked to use the CoaguChek®XS to measure their INR once every two weeks (or more often if requested by their GP) and report the result to their GP, as arranged, for dosage adjustment. The decision to alter warfarin doses was made by the patient's GP on the basis of the INR result. GPs were remunerated for the time involved in dosage adjustments informed by patient obtained POC INR results.

6.3.1.4 Development of educational materials

6.3.1.4.1 Train the trainer

A train the trainer package previously developed by the research team was used to train the accredited pharmacists participating in this project. This package included a training booklet to equip accredited pharmacists with the skills to train patients to successfully monitor their own therapy (Appendix 15). The booklet comprehensively covered anticoagulation theory, with topics ranging from the mechanism of action of warfarin and thrombosis to the therapeutic uses of warfarin and managing warfarin therapy. It covered the INR and the POC INR testing, as well as the accuracy of POC INR devices and the need for quality assurance. Finally, the book covered the evidence behind PSM of warfarin and training of patients to perform PSM. This resource was designed to be used as part of a training package that included oral presentations, practical demonstration of the CoaguChek®XS monitor and one-on-one demonstrations. The booklet was a support material for the oral presentations and a reference for accredited pharmacists training patients to monitor their own warfarin therapy. This tool was offered to the Project Advisory Group for independent review and refinement for use in this study. Additional tools were created to assist GPs and community pharmacists to identify suitable

candidates for PSM – these were incorporated into a flyer to encourage recruitment of patients into the project (Appendix 25).

6.3.1.4.2 Train the patient

As a component of the train the trainer package described above, the project team had also developed training materials for accredited pharmacists to use when training patients to perform PSM. The patient booklet was divided into two sections (Appendix 16). The first covered coagulation, how warfarin works, its therapeutic uses, the INR and the evidence behind self-monitoring and the POC devices. The second section covered quality assurance and was designed to incorporate the hands-on training session with the INR monitor. This package also underwent refinement before being offered to the Project Advisory Group for review. Additional resources for patients participating in the study were developed, including warfarin identification wallet cards and an INR record book (Appendix 6 and Appendix 10).

6.3.1.5 Recruitment of study participants

6.3.1.5.1 Pharmacy-Based Model Enabling Patient Self-Monitoring of Warfarin

6.3.1.5.1.1 *Pharmacist recruitment*

Pharmacists in Tasmania who had previously expressed an interest in participating in research projects were sent an invitation to participate in this study. A group of pharmacists in the Riverina region of NSW who had recently contacted the project team about participating in research projects were also approached to participate. Pharmacists practicing in 10 community pharmacies approved to claim for HMRs in the Hobart region of Tasmania and five in the Riverina region of NSW were engaged to participate and recruit patients for the implementation phase.

Pharmacists attended a training evening prior to the commencement of recruitment of patients in that region. Educational evenings were held in Tasmania in August 2008 and in Wagga Wagga in December 2008. These evenings provided participating community pharmacists with a refresher on anticoagulation theory, a background to self-monitoring as a strategy for warfarin management, and training on what was required from them during the project period. The pharmacists were also given a demonstration of the CoaguChek®XS device which was followed by a hands on session to ensure they fully understood the testing procedure they would be referring their patient to undertake.

Participating pharmacists were responsible for facilitating an HMR with a trained accredited pharmacist, via referral from the GPs. Pharmacists were provided with a list of trained accredited pharmacists in their area. Many of the NSW pharmacies had trained accredited pharmacists on staff.

Throughout the intervention, community pharmacists provided participants with support and ongoing education, as well as facilitating the ongoing supply of study materials to the patient from the project team.

6.3.1.5.1.2 *Accredited pharmacist recruitment*

Training sessions for accredited pharmacists wanting to up skill in the area of PSM were held by the project team as optional workshops at annual ConPharm conferences, with around 100 accredited pharmacists being trained across the country.

Accredited pharmacists who had previously attended such training sessions and who serviced the areas surrounding recruited pharmacies were contacted directly and invited to participate. Two accredited pharmacists in the Hobart region and one accredited pharmacist in the Riverina region responded. In Hobart, one accredited pharmacist was available to perform all necessary HMRs. An additional training

session was held in Wagga Wagga in December 2008 to up skill an additional five accredited pharmacists in this region.

Training sessions followed the contents of the train the trainer booklet, as described above, and covered anticoagulation theory and the evidence behind POC INR testing. This was accompanied by a practical training session on the use of the CoaguChek®XS device and included each pharmacist demonstrating their capability to obtain an INR result and describe the testing procedure to a patient.

Accredited pharmacists were required to provide HMR reports to the patient's pharmacy and GP, as is standard practice, and to make a recommendation on the patient's suitability to self-monitor based on a post-training assessment (Appendix 12).

6.3.1.5.1.3 *Recruitment of patients*

Patients were invited to participate by their community pharmacist. These patients had been taking warfarin for at least six months and had a long-term indication for warfarin therapy. Community pharmacists were given criteria to assist them to select potential candidates for PSM (Appendix 25).

The participating community pharmacists identified patients filling prescriptions for warfarin who they thought may be capable of and interested in self-monitoring their warfarin therapy. Patients with carers were not excluded from participating if they had an interest in self-monitoring and they had a carer who was willing and able to undergo training and perform INR testing on their behalf.

A range of strategies were used to identify patients, with some community pharmacists approaching patients when they presented in store, some posting letters to people they thought would be interested, and some choosing to work collaboratively with local GPs to identify potential participants. Patients then

contacted the project team, or asked their pharmacist to contact the project team on their behalf.

Once the patient consented to be involved in the study, the research team contacted the patient's GP informing them of the study and their patient's interest in participating. An information form and consent form were then sent to the GP. For a patient to be involved in the trial, their GP must also have provided consent.

6.3.1.5.2 The Role of Community Pharmacy in Post Hospital Management of Patients Initiated on Warfarin: Patient Self-Monitoring Phase

6.3.1.5.2.1 *Accredited pharmacist recruitment*

Accredited pharmacists who had participated in the intervention phase of the post-discharge project were invited to participate in this phase. Interested accredited pharmacists were trained in the PSM phase of the project via completion of the Anticoagulation Education Program described above and attendance at training sessions conducted in Hobart and Adelaide in October 2009.

6.3.1.5.2.2 *Recruitment of patients*

Patients identified during the intervention phase of The Role of Community Pharmacy in Post Hospital Management of Patients Initiated on Warfarin project through the Tasmanian and South Australian study sites were assessed for their willingness and capability to self-monitor. They included both patients newly initiated on warfarin and those who were admitted to hospital on the drug. The assessment included an evaluation of additional health conditions (e.g. additional diagnoses, problems with visual acuity and manual dexterity, and the need for assistance with daily activities as described above). Patients were also questioned on their interest in participating in PSM, including training. If patients consented to participating in training and seemed eligible, they were referred to their GP for discussion and GP consent.

6.3.1.5.3 Long-Term Follow-Up

6.3.1.5.3.1 *Patient recruitment*

Existing participants of the above studies were invited to extend the duration of their participation in PSM research for a further six to 12 months. Patients and GPs were provided with revised information forms and were required to complete a new consent form to cover the additional PSM phase.

A small number of additional patients had approached the project team during the study period and an extension of ethics was obtained to enable their recruitment into the project at this point. These patients and their GPs also provided consent.

6.3.1.6 Implementation of the self-monitoring model

6.3.1.6.1 Experimental design and analysis of results

These projects were designed as proof of concept studies regarding the implementation of pharmacist involvement in PSM of warfarin therapy in the community. The main outcomes examined the impact of PSM on INR control, calculated as TTR.

Data on clinical outcomes, such as minor and major bleeding, were collected, but it was not anticipated that improvements would be observed in this study due to a small sample size and relatively short time-frame. Minor bleeding was defined as bleeding that was reported but not requiring additional tests, referrals and visits, while major bleeding was categorised as including fatal or life threatening bleeding, or bleeding associated with a defined drop in haemoglobin and requiring transfusion.[12]

Patients were required to successfully complete two comparison INR tests with pathology results to ensure that they could operate the monitor in a competent manner and obtain accurate results.

The TTR and proportion of tests within target range of INR were determined for each patient during the trial. This was compared to their previous level of control determined in the six months immediately prior to the commencement of the intervention phase (provided at study entry with the participant's consent).

Target INR ranges are generally taken to be within 0.5 of the target INR value.[230] Specifying tighter target ranges for fully anticoagulated patients has been demonstrated to result in more blood tests and more INR results in ranges associated with increased risk of thrombosis and bleed, without actually achieving tighter control.[367] TTR values for this study were calculated using the literature recommendations for the target ranges for each of the conditions for which warfarin was prescribed. A range of 2.5-3.5 was used for patients with mechanical heart valves,[53] for all other indications a range of 2.0-3.0 was applied.[12]

A function to calculate the TTR was based on the method originally proposed by Rosendaal et al.[348] Based on this calculation, the TTR for each participant was determined for available pre-intervention and intervention data. Data regarding TTR and proportion of tests in range approached normality and as such was treated as parametric. POC INR comparisons with laboratory results were also normally distributed. Paired t-tests were used to analyse the comparisons. Due to the small sample size, all other data was treated as non-parametric and Wilcoxon signed rank sum tests were used for comparisons. Statistical significance was set at p less than 0.05.

6.3.1.6.2 Quality of life

Due to the difficulties associated with quantifying the benefits of an intervention program, a common unit of measurement for benefit, quality of life (QOL), was utilised. QOL was measured using the EQ-5D instrument (Appendix 26), which comprises five dimensions of health (mobility, personal care, usual activities,

pain/discomfort, anxiety/depression) with respondents being offered the choice of three 'levels' under each dimension ('no problems', 'some/moderate problems', and 'extreme problems'). The questionnaire was conducted with each patient twice, at entry into the study and following the intervention. The results for the participants' EQ-5D were entered into a database. The UK 'Time Trade Off' (TTO) data set was utilised to calculate a utility weight for each participant before and after PSM. No Australasian data set is currently available, and the UK TTO data set has been used previously in the Australian context.[368] (Note: TTO involves asking a person to imagine living in a specified health state for 10 years and then asking them to specify the amount of time they would be willing to give up to live in 'full health' instead.[369]) This instrument was selected for use prior to the author becoming involved in this project, during the funding application. It had also been selected for use in the The Role of Community Pharmacy in Post Hospital Management of Patients Initiated on Warfarin project. While it was not expected to be sensitive enough to pick-up small differences in quality of life in such a small sample of patients, it was retained for use to allow comparisons to be made between the baseline results of patients in both project groups. Participants' pre- and post-PSM utility weight results were compared using the Wilcoxon Signed Ranks Test. Statistical significance was set at p less than 0.05.

6.3.1.6.3 Warfarin knowledge

Participants completed the Oral Anticoagulation Knowledge (OAK) Test (Appendix 27).[370] The questionnaire was completed at study entry and again on completion of the study. For the Pharmacy-Based Model Enabling Patient Self-Monitoring of Warfarin project, the questionnaire was completed at study entry, in the post-training period (at approximately two to four weeks following the HMR), and again on completion of the original six month PSM phase. It was also completed at the conclusion of the long-term follow-up study.

Scores were calculated as a percentage and participants were awarded a pass or fail score based on this, with the pass mark being set at 72.4%.[371] Wilcoxon signed rank sum tests and Friedman tests for non-parametric data were used to compare warfarin knowledge levels at various time points. Independent samples T-tests were used to explore the relationship between knowledge and INR control. Statistical significance was set at *p* less than 0.05.

6.3.1.6.4 Sample size

For the Pharmacy-Based Model Enabling Patient Self-Monitoring of Warfarin project, a sample size of 20 to 30 patients was deemed to be adequate to demonstrate the feasibility of this model of warfarin management. Participants involved in the study were required to have had at least six months of warfarin therapy prior to the study, and INR results from this period were provided to the research team as part of the patient enrolment in the trial. It was presumed that participants would have had six to 12 INR results in this period. During the study period, participants were anticipated to complete at least 12 INR results. For 30 patients, 360 pre-study INRs and 360 in-study INR results were anticipated. The literature suggests that patients in the community spend 50-60% of their time within the target range.[56] It was envisaged that this could be improved to 70% with weekly testing and improved education, although an improvement of 5-10% has been proposed as a clinically important goal.[51] At a power of 80% and statistical significance set at 0.05, 175 INR results per group were required to achieve significance.

The study was not powered to detect clinical outcomes, although their occurrence was documented as a matter of course. It should be emphasised that the over-arching objective of the study was to demonstrate that the proposed clinical pathway for PSM was feasible and patients, pharmacists and GPs were satisfied with

this model of care. It was intended that the process would allow issues with the training procedure to be identified and aid in its refinement. The primary outcome for the analysis of the implementation phase of the project was TTR. Secondary outcomes included improvement in warfarin knowledge and QOL.

6.3.1.7 Handling of data

All data was treated confidentially and anonymously. The names of participating patients were not stored with questionnaires or data files on computer.

6.3.1.8 Statistical analysis

Recruited patients were analysed for changes in quality of INR control on an intention-to-treat basis. That is, the results of patients who did not complete the long-term follow-up phase were included and analysed as part of this group.

Paired samples t-testing was utilised for continuous variables and McNamer's test for discrete variables when comparing before and after data. Where a low number of responses failed to permit the use of parametric statistics, non-parametric statistics were utilised with medians and ranges, and Fisher's exact test for discrete variables reported. A p value of <0.05 was specified as statistically significant for all analyses.

All information was stored and analysed using SPSS 18.0 for Windows (SPSS Inc. Chicago, Illinois, USA).

6.3.1.9 Ethical approval

The Pharmacy-Based Model Enabling Patient Self-Monitoring of Warfarin project received ethical approval from the Tasmanian Health and Medical Human Research Ethics Committee (H0009825) and the Human Research Ethics Committee (University of Sydney) (09-2008/10955) and was registered with the Australian Clinical Trials Registry (ACTRN 12608000374369)

The Role of Community Pharmacy in Post Hospital Management of Patients Initiated on Warfarin: Patient Self-Monitoring Phase project received ethical approval from the Tasmanian Health and Medical Human Research Ethics Committee (Approval Number: H0010105) and the University of South Australia Human Research Ethics Committee (P252/08) and was registered with the Australian Clinical Trials Registry (ACTRN 12608000334303)

The Long-Term Follow-Up project received ethical approval from the Tasmanian Health and Medical Human Research Ethics Committee through amendments to previously approved applications.

6.3.2 Exploration of Patient Views of Self-Monitoring of Warfarin

Qualitative research methods enable the exploration of different research questions to those that can be addressed by quantitative methods. Qualitative research approaches "seek to uncover the thoughts, perceptions and feelings experienced by informants",[372] attempting to make sense of, or interpret, phenomena in terms of the meanings that people bring to them.[373] They place emphasis on the meanings, experiences, and views of all the participants and can explore aspects of complex behaviours, attitudes, and interactions which quantitative methods cannot.[374] In the context of PSM of warfarin, quantitative methods can describe what happens to INR control, and the potential impact this may have on clinical outcomes, while qualitative methods enable the exploration of patient-centred outcomes resulting from PSM.

Qualitative methods do not seek to provide quantified answers to research questions.[374] They involve the collection of data in the form of talk and observation to be described and explained, while quantitative methods generally collect data which may be statistically analysed in some way.[361] Qualitative methods do not set out to deductively test a predefined hypothesis, but rather to inductively develop a hypothesis from the data collected.[361] They also recognise the researcher as a participant in the research whose own views and values will impact, to some degree, on the data collected, while quantitative methods require the researcher to remain objective and independent during data collection and analysis.[375] Despite their seeming polar opposites, in some situations, combining the two approaches provides the most comprehensive answer to a research question.[374]

6.3.2.1 Mixed methods research

To provide a greater depth of evidence to support PSM, a mixed methods research approach was adopted. Mixed methods research is a methodology that involves

collecting, analysing and mixing qualitative and quantitative approaches throughout the research process.[376] To be effective, mixed methods research relies on the presence of a deliberate relationship between the two approaches to ensure that the data can be used to produce greater insight than if a single approach was used.[377] Creswell and Plano Clark define mixed methods research as:

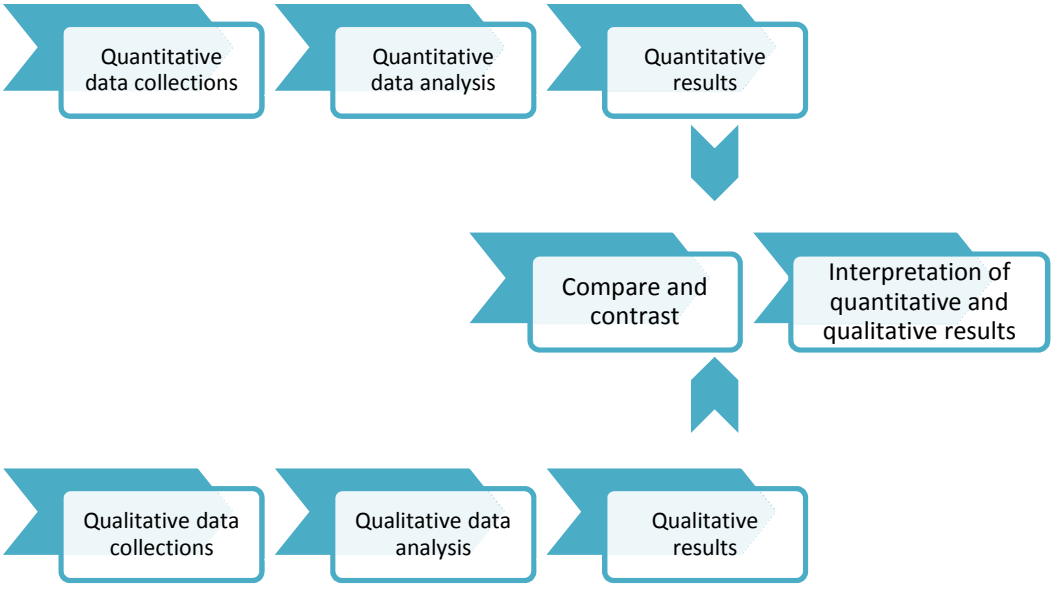
> *…a research design with philosophical assumptions as well as methods of inquiry. As a methodology, it involves philosophical assumptions that guide the direction of collection and analysis of data and the mixture of qualitative approaches in many phases of the research process. As a method, it focuses on collecting, analysing, and mixing both quantitative and qualitative data in a single study or series of studies. Its central premise is that the use of quantitative and qualitative approaches in combination provides a better understanding of research problems than either approach alone.*[376]

Mixed methods designs can be used when a need exists for both quantitative and qualitative data to adequately address a research problem.[376] For some research questions, the combination of the two types of data can provide a more complete picture of the story being researched than a single data type alone.[376] In this study, it was felt that using a mixed methods approach and integrating qualitative and quantitative data, would provide objective evidence on the practice of PSM that would be enriched by the lived experiences of the self-monitoring participants.

Data can be combined in a number of ways, using four major types of mixed methods designs.[376] For this study, a triangulation design was adopted. The purpose of triangulation is to "obtain different but complementary data on the same topic".[378] It involves collecting quantitative and qualitative data during the same study, giving equal weighting to the data obtained from each method, and merging the data during interpretation or analysis.[376] Data in this study was converged

during interpretation in an attempt to develop valid and well-substantiated conclusions about the phenomenon of PSM.[376] Figure 28 demonstrates the convergence model of triangulation design.

Figure 28: Triangulation Design: Convergence Model (adapted from Creswell and Plano Clark[376])



6.3.2.2 Research questions

The collection of qualitative data and the subsequent analysis was guided by the following research question:

How are patients experiencing and perceiving self-monitoring?

Within the parameter of this research question, particular attention was focussed on the ways that self-monitoring may have changed:

- Autonomy and independence
- Perceptions of quality of life
- The experience of living with a chronic illness

- Perceptions of self-efficacy
- Views on taking warfarin

6.3.2.3 Methodological approach

The methodology for this study draws upon the interpretive tradition. Because one of the aims of this study was to explore the experiences and perspectives of individuals undertaking PSM, an interpretive qualitative inquiry, which allows for focus on the meanings that participants give to their actions, to the actions of others, and to the social context, in which participants live was considered the most suitable methodological framework for this component of the study.[363]

Some of the methodological traditions provided by grounded theory have also been drawn upon for this study. Grounded theory is an example of an interpretive and iterative approach that attempts to derive theories and develop a deeper understanding 'grounded' in detailed systematic analysis of the data.[377, 379] Grounded theory is an inductive research technique that focuses on the meanings and interpretations of research participants emerging from their descriptive accounts, rather than being guided by a firm hypothesis.[361] It is an appropriate methodological approach to undertake when studying experiences of participants and explaining processes.[377] It is not an approach that may be used to test or verify existing understandings of processes.[377]

Grounded theory is an approach that includes precise and specific guidelines and procedures for producing grounded theories many of which were not adopted in this study.[379] However, key features of grounded theory were utilised in this study. These features are, an iterative study design, purposive sampling, the intent to develop concepts and theory from the data and the use of coding in data analysis.[380]

The iterative study design involves cycles of simultaneous data collection and analysis, where the analysis sharpens the focus of future data collection.[380]

6.3.2.3.1 Interviewing as a means of data collection

6.3.2.3.1.1 *Justification for the use of interviews*

Qualitative in-depth interviews are largely unstructured.[364] Despite the lack of formal structure present in in-depth interviews, the interviewer is still aware of the issues or topics they are interested in pursuing and will often ask a participant to clarify or expand on issues discussed.[361]

Interviews are the most widely used qualitative data collection method.[361] Advantages of this form of data collection include the flexibility of the method, the ability to capture participants' own words, and for the researcher to spend some time interacting with participants.[361] Despite the advantages, there are also some disadvantages to collecting interview data. These include it being a very labour intensive data collection method and a method which requires quality recording equipment and some degree of training.[361]

6.3.2.3.1.2 *In-Depth interviews*

In-depth interviews are widely accepted as a method which enables the researcher to collect information about the ways that people understand the experiences of their lives,[363] and have the added advantage of facilitating a deeper understanding of the participants' experiences than other interview styles.[361, 381] The aim is to explore issues in as much detail as possible and to uncover new areas or ideas that may not have been expected at the outset of the research project.[382] Hansen describes in-depth unstructured interviewing as:

> *…a method stemming from perspectives such as phenomenology and narrative theory, where researchers want to understand the meanings people give to their*

> *experiences, to study the stories they tell and to place these in context. Therefore, the purpose of in-depth interviews is not to get answers to questions or to evaluate or test hypotheses. Instead in-depth interviews reflect an interest in understanding other people's experiences and the meanings they attribute to those experiences.*[361]

In-depth interviews have been used to explore patient perspectives in a range of applied health disciplines, including how people manage living with the consequences of chronic illness,[383, 384] how people perceive taking warfarin,[272, 273] people's perspectives on blood glucose testing in diabetes,[277] and ideas about medicines, medication management and medical decision making.[385-389] As such, in-depth interviews were chosen as the data collection method for this study to allow participants to describe their experiences with PSM and the effects this monitoring technique may have had on the way they manage their health.

Collecting data through in-depth interviews allows participants to give a description of self-monitoring which they can be prompted to expand upon as the interview progresses.[390] Conversational probes are used by the interviewer to clarify and further develop details raised by the interviewee.[382] Patton[390] describes probes as performing three main functions during an interview. They give cues to the interviewee as to the level of depth the interviewer wants in their response, may be used to deepen the response to a question, and assist in increasing the depth and richness of information interviewees provide in their answer.[390] Follow-up questions are often used in combination with probes, based on the interviewees' previous statements.[382] They are used in some cases to pursue themes, to elaborate the context of answers, and to explore the implications of responses.[391] Probes were used in this study to elaborate on points that were raised by participants during their narrative responses to the main question.

6.3.2.4 Sample

Sampling in qualitative research is not concerned with ensuring that the findings can be statistically generalised to the whole population, rather it is often purposeful and described as a non-probability sampling technique.[363] The aim of qualitative research is generally to describe the processes involved in a phenomenon, such as self-monitoring of the INR, and purposive sampling will aim to identify cases that will allow a full and sophisticated understanding of all aspects of INR self-monitoring.[364] The aim is to select information-rich cases for studying in depth.[364] In this study, the sample consisted of participants of the previously described trials of PSM. Participants who were no longer undertaking PSM were also included to ensure that as broad a range of self-monitoring experiences as possible could be explored. All available participants were interviewed and every effort was made to include all participants in the interview process, though a small number were unavailable.

As the participants of the PSM projects were already engaged in the research projects, they were recruited to participate in the interview process over the telephone. Their ongoing involvement in this research meant that the participants were generally eager to participate in the interview and the recruitment process was without difficulty. The reasons for doing the interviews were explained at this time. Consent to participate in the interviews had been provided at the commencement of the PSM projects.

6.3.2.5 The use of interviewing in this study

A key component to conducting effective interviews is establishing a rapport with the participants.[381] For many researchers this requires a period of informal interaction on arrival at the interview to enable the researcher to gain the participant's trust.[381] This is particularly important for interviews conducted from

an interpretive perspective, where interviewers are seen as active participants in the research and the meanings arising from the interview are collaboratively constructed by both the interviewer and interviewee.[392] The preceding PSM projects resulted in the researcher having had between six months and two years contact with the interviewees on a fairly regular basis. This contact enabled the researcher to develop a strong rapport and pre-existing background knowledge of the participants prior to the actual interview. Most interviews were conducted by the researcher face to face at the participant's house, as it is said that the setting of an interview may affect the content and it is preferable to interview people at home.[382] There were a few exceptions; three interviews were held at the participant's workplace, one at the researcher's workplace, and one in a café of the participant's choice, all at the participants' request. While face to face interviews were the goal, logistical issues such as time constraints and distance resulted in four interviews being conducted over the phone. At each face to face interview, the researcher arrived with a copy of the discussion guide, a notebook in which to jot any topics to be returned to at a later point in the interview and a digital voice recorder. The first few minutes were spent catching up with the interviewee, and their spouse or family where appropriate. Generally, the interview guide was put to one side and only referred to when the conversation lulled and further questions were expected by the interviewee. The notebook proved to be unnecessary during the interviews. A similar procedure was followed for the telephone interviews.

Despite the absence of a formal set of interview questions like those used in structured interviews, in-depth interviews may still utilise an interview guide or topic list.[390] Interview guides are generally used to outline a set of issues that the researcher wishes to explore during the interview and serves as a checklist for the researcher during the interview to ensure all the relevant topics of interest are covered.[390] They also help to ensure that the same basic lines of inquiry can be

pursued with each interviewee,[390] though usually in different ways and through the use of different probes. The interview guide used for this study can be seen in Figure 29.

Figure 29: Interview guide

Start with:

"Can you tell me about monitoring your own INR?"

Hopefully this will prompt a bit of a narrative… Will then be able to probe further on any interesting points raised during the narrative (will make little notes on the page to remind me)

Then, if not already covered, will ask things like:

"Have things improved since starting self-monitoring?"

"What was it like before you started self-monitoring?"

"What would it be like if you have to stop self-monitoring?"

"Has self-monitoring changed your confidence about managing warfarin?"

Also want to look at:

The educational advice and training provided

Experiences with using the device

Any changes in relationships with pharmacists and GPs

Experiences with the website (where applicable)

6.3.2.6 Analysis of interview data

Iterative data analysis is a mode of analysis that forms the basis of analysis for methodologies such as grounded theory or phenomenology, placing it as an analytical approach within the interpretive tradition.[363] Grounded theory utilises a very specific three stage coding process as part of its analysis, while phenomenology involves a unique process of data collection and analysis.[363] Grounded theory emphasises steps and procedures for connecting induction and deduction through

the constant comparative method.[390] Outside of these methodologies, iterative approaches adopting the constant comparative method are still widely used, particularly in applied health research, and enable data collection and analysis to occur in tandem.[361] Such iterative processes involve a succession of question and answer cycles where researchers consciously move between analysing and collecting new data.[361, 393] They involve collecting information in the field, for example through interviewing, transcribing this information, reflecting upon it and subjecting it to an initial analysis, then using this information to guide the next round of data collection.[363]

Iteration is primarily an inductive process where points of interest are identified within the data rather than being guided by pre-established ideas.[361] To generate these categories or move deeper into the analysis process, researchers identify interesting sections of the data, be it words, phrases or sentences, and then mark and label them in a process known as 'coding'.[361, 376] Coding helps researchers identify new issues arising from the data by changing the researcher's relationship with the data and facilitating a process of reflection and discovery.[361] It is also a method of grouping evidence and labelling ideas so that they begin to reflect increasingly broader perspectives.[361, 376] These broader perspectives of recurring issues may be used to describe themes that emerge from the data.[361]

Data collection and analysis were performed concurrently throughout the interview period and an iterative approach to data analysis was adopted. As previously described, the interviews were digitally recorded. Transcription of the recording was outsourced and analysis began while checking the transcriptions of these recordings. The transcriptions were printed out in hard copy to enable corrections to be made as the recordings were reviewed. Corrections were then made to electronic copies and a second hard copy printed out and checked. Preliminary

analysis and coding is recommended to be undertaken by hand prior to any data manipulation being done on a computer.[363] As such, the copies of the transcripts were read and interesting passages and phrases were marked and annotated (coded). The electronic copies of the transcripts were imported into NVivo 8 software (QSR International Pty Ltd, Doncaster, Australia) where coded passages from the hard copies were transferred into the program. These codes were able to be labelled, filed and stored electronically, enabling easy retrieval at a later point.

The codes arising from this process included are shown in Table 23.

As the interviews progressed and the analysis of the transcripts continued these codes were compared to identify like and unlike issues arising from the data. A second investigator was employed to read the analysis of themes and corresponding parts of the transcripts. This investigator came from a divergent background and disciplinary expertise, being a sociological researcher, with little experience in the discipline of pharmacy. They participated in discussions on the content of the interviews, prompting critical reflection of the analysis process that was being undertaken and improving the rigour of the process.

Recurring codes were then able to be grouped into themes within the software program. NVivo enables the construction of hierarchical structures of themes and codes. The themes were constructed around the organising framework of how participants were talking about INR self-monitoring. The themes identified were:

> *Confidence; Convenience; Descriptions of PSM Empowerment; Healthcare professionals; INR control; Perceptions of warfarin;*

Many of the codes outlined above were grouped within these themes. Some sections of transcripts related to more than one code so some sections of transcript

sometimes appeared under more than one theme. The final coding structure within the themes is shown in Table 23.

Table 23: Coding structure

Theme	Corresponding codes
Confidence	Ability to improve INR control Ability to learn & monitor interactions Accuracy of PSM vs. usual care Adjust own treatment Check if INR out of range Concomitant illness Improve outcomes Testing frequency
Convenience	Ability for self-transport Adverse effects of usual care Affordability of PSM to self Affordability of PSM to heath care system Compliance with testing Distance to usual care site Impact on other activities Interruptions to therapy Level of usual care On the spot Time to get usual care result
Descriptions of PSM	Words used to describe PSM Comparisons
Empowerment	Control over health Desire to recommend PSM Ability to adjust dose Freedom from usual care Reduced anxiety Freedom to do Participation in research
Healthcare professionals	Descriptions of GPs Descriptions of pharmacists
INR control	Doctor's directive for INR control Target INR Experience with out of range results Degree of INR fluctuation Compliance with warfarin Perceived importance of INR control Procedure with usual care
Perceptions of warfarin	Routine with taking warfarin Danger & uncertainty Explanation by health professional at start Inability to know risk of side effects Perception of warfarin Prefer risk over stroke Previous experience with events Words to describe warfarin

NVivo allowed each code and the corresponding sections of the transcripts to be extracted from the program and printed out. These print outs were then used to enable further checking of the material grouped under each code. At this point, some codes containing few sections of transcript were merged with other similar codes if appropriate. This process also allowed the identification of any material which may have been assigned to the wrong code and for this data to be recoded.

One feature of iterative thematic analysis is the amalgamation and subdivision of themes which occurs before the final interpretation and writing up process begins.[363] At this stage of analysis it was identified that the themes could benefit from a process of further refining. After studying the themes and their corresponding codes it became apparent that participants talked about two main issues during their discussions. They talked in detail about what their lives were like before they had the ability to perform self-monitoring, including what the INR testing procedure was and how they felt about taking warfarin, and they discussed how this had changed now that they were testing their own INR, generally comparing the two models of care. Thus, the themes were amalgamated under higher level themes of 'Taking warfarin', to describe what taking warfarin was like prior to self-monitoring, and 'Comparing PSM to usual care', to describe what and how things had changed with self-monitoring.

Taking Warfarin	**Comparing PSM to usual care**
Perceptions of warfarin	*Perceptions of PSM*
Importance of INR control	*Descriptions of the role of*
Procedures of usual care	*healthcare professionals in PSM*
	Convenience
	Confidence
	Empowerment

The act of writing the chapter completed the analysis.

6.4 Results

6.4.1 Pharmacist-Based Model Enabling Patient Self-Monitoring of Warfarin

6.4.1.1 Participants

A total of 48 patients completed the initial training program and were evaluated for control of their INR.

6.4.1.1.1 Pharmacy-Based Model Enabling Patient Self-Monitoring of Warfarin

Twenty-eight patients completed the initial training program and went on to participate in this phase of the study. A further four patients approached the project team to participate but were not successfully recruited into the project. Reasons for non-recruitment were:

- GP factors (n=2): in both cases the patient's GP refused consent; and
- Patient factors (n=2): One patient did not feel confident with the responsibility of performing testing and one patient was found during the HMR to have a diagnosis of lupus anticoagulant (contraindications to POC INR monitoring in patients suffering from lupus anticoagulant or antiphospholipid syndrome according to the CoaguChek®XS product information[394])

Thirty GPs were involved in the management of the recruited patients, though some GPs were responsible for multiple patients and some patients had multiple GPs during the trial period. Patients were recruited through 13 community pharmacies – 10 in Tasmania and three in New South Wales.

Two patients were unable to continue self-monitoring for the six-month duration. One patient was unable to be contacted and was removed from the study, the other passed away during the intervention period due to unrelated causes (acute

myocardial infarction with therapeutic INR). The data from these patients was included in the long-term follow-up study. All recruited patients were capable of completing training and using the monitor. Similarly, no patients were excluded by their GP once the study commenced. Two elderly patients had a carer present at the training session that they preferred to perform the testing procedure on their behalf.

6.4.1.1.2 The Role of Community Pharmacy in Post Hospital Management of Patients Initiated on Warfarin: Patient Self-Monitoring Phase

Sixteen patients completed the initial training program and went on to participate in this phase of the study. A further 29 patients were approached by the project team to participate but were not successfully recruited into the project. The flow of patient recruitment can be seen in Figure 30. Reasons for non-recruitment were:

- GP factors (n=8): including the GP not providing consent and the GP not supportive of the project;
- Duration of therapy (n=4): including patient having ceased warfarin or having an expected duration of therapy remaining of less than three months; and
- Patient factors (n=17): including a lack of confidence with performing testing, preference for usual care, going overseas, concerns regarding accuracy, no longer interested in participating, and personal circumstances including further episodes of hospitalisation.

Sixteen GPs were involved in the management of the recruited patients. Patients were recruited through the Hobart (n=7) and Adelaide (n=9) project sites.

All patients who completed training continued to perform PSM for the three-month duration of the study. All recruited patients were capable to complete training and

use the monitor. Similarly, no patients were excluded by their GP once the study commenced.

6.4.1.1.3 Long-Term Follow-Up

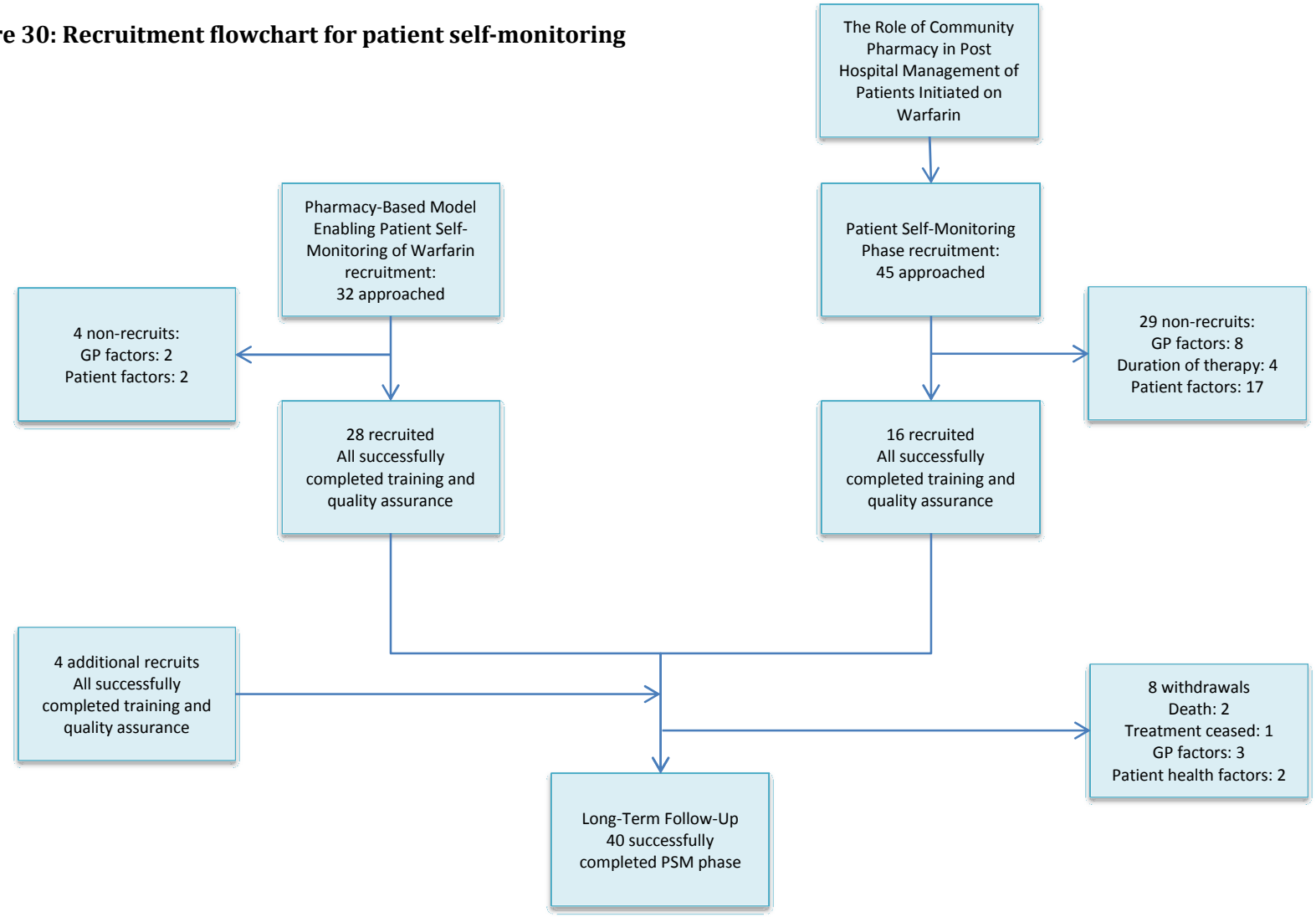
All patients in the preceding PSM phases consented to participate in the long-term follow-up phase; however, two patients were refused consent by their GPs to continue. Reasons for GP non-consent were:

- Patient factors (n=1): patient not attending surgery regularly enough for GP preferences; and
- GP factors (n=1): lack of confidence in the machine.

An additional four patients from South Australia (n=1) and Tasmania (n=3) approached the project team during the preceding phases and provided consent to join the project at this stage.

Four patients were unable to continuing self-monitoring for the duration of the long-term follow-up. Two patients suffered significant health problems (cancer related (n=1) and intracerebral haemorrhage with therapeutic INR (n=1), one patient ceased taking warfarin and was unable to complete the study, and another passed away during the follow-up period due to unrelated causes (acute myocardial infarction with therapeutic INR).

Figure 30: Recruitment flowchart for patient self-monitoring



6.4.1.2 Patient characteristics

Table 24 displays the patient characteristics for enrolled patients. The majority of patients (60.4%; 29 of 48) were male. AF was the most common indication for warfarin therapy and a target INR range of 2.0-3.0 was the most common.

Table 24: Patient characteristics

	Overall (n=48)
Male gender (%)	29 (60.4)
Median age (range)	64.7 years (22.2 – 88.9 years)
*Indication for warfarin**	
AF (%)	24 (56.3)
Recurrent VTE (%)	14 (29.2)
Mechanical heart valve (%)	8 (16.7)
Stroke (%)	4 (10.4)
Other (%)	6 (12.5)
Target INR range	
2.0 – 3.0 (%)	36 (75.0)
2.5 – 3.5 (%)	6 (12.5)
Other (%)	6 (12.5)
State	
NSW (%)	8 (16.7)
SA (%)	10 (20.8)
TAS (%)	30 (62.5)
Region	
Major city of Australia (%)	9 (18.8)
Inner Regional (%)	32 (66.7)
Outer Regional (%)	5 (10.4)
Remote Australia (%)	0 (0.0)
Very Remote Australia (%)	2 (4.2)

** some patients listed more than one indication for warfarin.*

At commencement of self-monitoring the median duration of warfarin therapy was 3.9 years (range 0.1 to 35.0 years).

6.4.1.3 Proportion of time within target INR range

Complete INR data sets were available for 46 of the 48 participants. The mean TTR at baseline was 64.0% (95% CI 55.0% to 73.1%). A total of 366 INR tests were provided in the six months prior to the initiation of PSM.

Patients performing PSM subsequently spent a mean TTR of 72.9% (95% CI 67.5% to 78.3%). A total of 1977 home tests were completed by the group during the PSM phase and participants undertook a median of 16.9 (range 2.7 to 24.9) months of PSM. The improvement in TTR when patients performed PSM was statistically significant (p=0.038). These results are shown in Table 25.

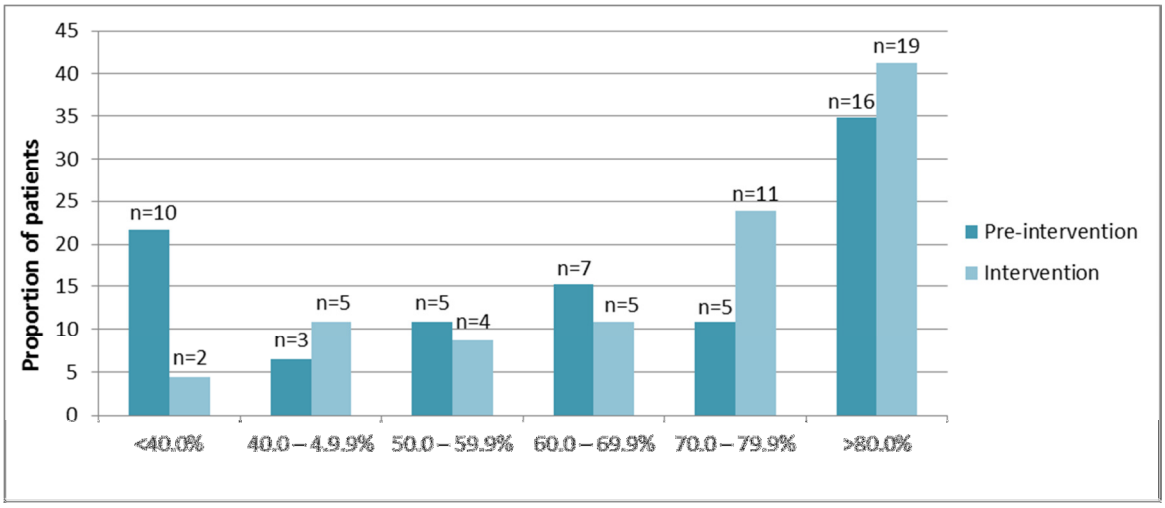
Table 25: Quality of anticoagulation pre- and post-intervention

	Overall (n=46)	
Mean percentage TTR (95% CI)		
Pre-intervention TTR	64.0 (55.0 - 73.1)	t= -2.14; df= 45; **p=0.038***
Intervention TTR	72.9 (67.5 - 78.3)	
Mean percentage time below therapeutic range (95% CI)		
Pre-intervention time below range	22.6 (13.9 – 31.3)	t= 0.81; df= 45; p=0.421
Intervention TTR time below range	19.2 (13.8 – 24.6)	
Mean percentage time above therapeutic range (95% CI)		
Pre-intervention time above range	13.0 (7.2 – 18.9)	t= 2.01; df= 45; p=0.050
Intervention TTR time above range	7.7 (5.3 – 10.1)	

* Findings in **bold** indicate statistical significance.

Figure 31 shows a summary of the distribution of the mean TTR.

Figure 31: Overall INR control



The change in TTR during the PSM period was compared for patients when grouped according to INR control in the pre-intervention period (Table 26). A TTR of 60% is said to be an important clinical goal for people taking warfarin,[61] while a TTR of >80% is classified as excellent control.[62] Patients who initially had sub-optimal INR control (<60% TTR) benefited significantly more from PSM than those with good (60 – 80% TTR) or excellent (>80% TTR) INR control in the pre-intervention period, with a median improvement in INR control of 29.6% (range -2.9 to 85.2%); F (2,43) = 19.242, p <0.001 (Figure 32).

Table 26: Change in TTR with self-monitoring

Pre-intervention TTR	Median change with PSM (range)	*p*
<60.0%	29.6 (-2.9 – 85.2)	<0.001
60.0-80.0%	5.9 (-35.1 – 15.9)	
>80.0%	-7.3 (-58.6 – 4.0)	

Figure 32: Median change in INR control with self-monitoring

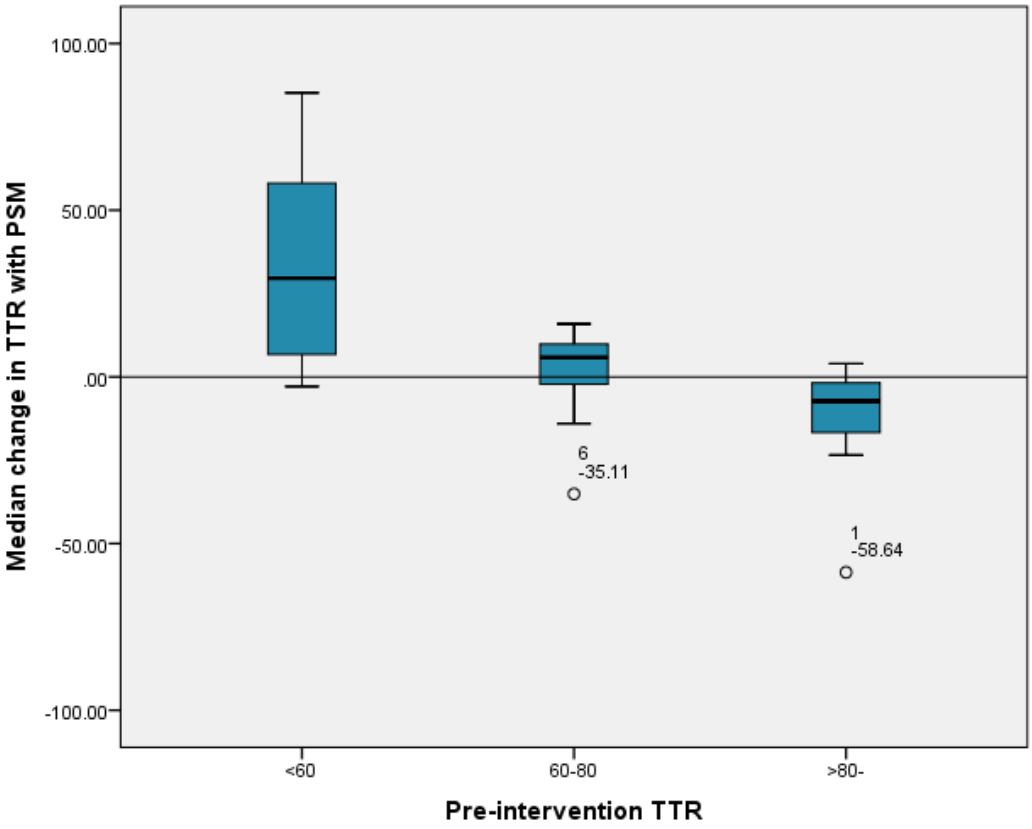


Table 27 shows a breakdown of the TTR for Australian states and territories. There were no significant differences in the changes in TTR for patients within each state.

Table 27: INR control by state

Median percentage TTR (range)	**Overall (n=46)**	***P***
NSW (n=8)		
Pre-intervention TTR	79.7 (0.0 – 100.0)	0.499
Intervention TTR	80.3 (30.9 – 89.6)	
SA (n=10)		
Pre-intervention TTR	61.0 (43.2 – 100.0)	0.889
Intervention TTR	67.3 (41.4 – 89.6)	
Tas (n=30)		
Pre-intervention TTR	67.4 (0.0 – 100.0)	0.074
Intervention TTR	76.9 (26.3 – 100.0)	

Table 28 shows a comparison of TTR by region. There were no significant differences in the changes in TTR for patients within each region.

Table 28: INR control by region

Median percentage TTR (range)	**Overall (n=46)**	***p***
Cities of Australia (n=9)		
Pre-intervention TTR	65.0 (48.7 – 100.0)	0.176
Intervention TTR	59.9 (41.4 – 80.0)	
Inner Regional (n=32)		
Pre-intervention TTR	76.5 (0.0 – 100.0)	0.050
Intervention TTR	80.9 (26.3 – 100.0)	
Outer Regional (n=5)		
Pre-intervention TTR	56.4 (0.0 – 100.0)	0.465
Intervention TTR	65.9 (54.7 – 96.4)	
Very Remote Australia (n=2)		
Pre-intervention TTR	50.5 (43.2 – 57.7)	0.180
Intervention TTR	77.0 (64.5 – 89.6)	

There was no significant difference between the INR control of those patients who utilised the web-based monitoring platform (described in Chapter 4) and those who did not (67.8% vs. 73.4% respectively; p=0.584).

6.4.1.4 Testing frequency

The frequency of INR testing was a mean testing frequency of 1.3 (95% CI 1.0 to 1.6) tests per month in the six months prior to self-monitoring. During the self-monitoring period the frequency of testing significantly increased, with a mean testing frequency of 2.9 (95% CI 2.4 to 3.3) tests per month (t = -7.29; df = 46; p <0.001). These results are shown in Table 29.

Table 29: INR testing frequency

Testing frequency	**Mean (95% CI)**	
Tests per month pre-intervention	1.3 (1.0 - 1.6)	t= -7.29; df= 46; p<0.001
Tests per month post-intervention	2.9 (2.4 - 3.3)	
Testing interval (days) pre-intervention	26.7 (19.4 - 33.9)	t= 4.46; df= 43; p<0.001
Testing interval (days) post-intervention	11.7 (10.0 - 13.4)	

6.4.1.5 Accuracy of the CoaguChek®XS portable INR monitor

A total of 177 comparison INRs (CoaguChek®XS and pathology INR within four hours of each other) were completed either on entry into, or during the trial, by participants. The CoaguChek®XS INR values were significantly correlated with the laboratory INR values (r=0.94, p<0.001; Figure 33). The mean difference in INR (laboratory minus CoaguChek®XS) was 0.07 ± 0.02 INR units (t=4.37, df=176, p<0.001). As a requirement of entry into the trial, patients were required to complete two comparison INRs, with the values being within 15%. The Bland-Altman style plot is shown in Figure 34. The CoaguChek®XS showed only slight variation compared with laboratory testing, with a mean variation of 6.4% ± 0.41%.

Figure 33: Relationship between CoaguChek®XS and laboratory INR values

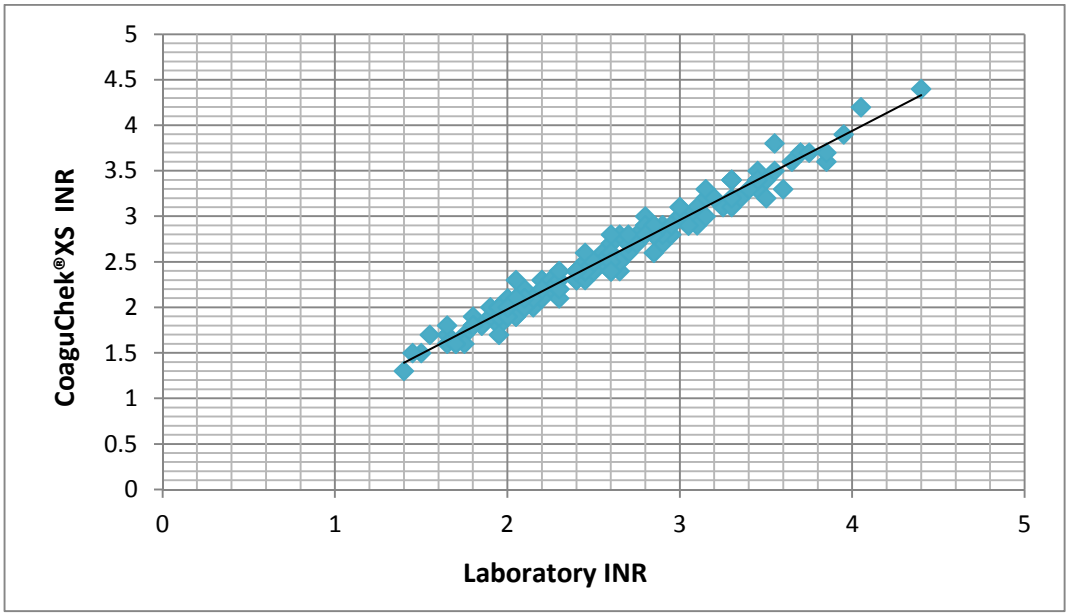
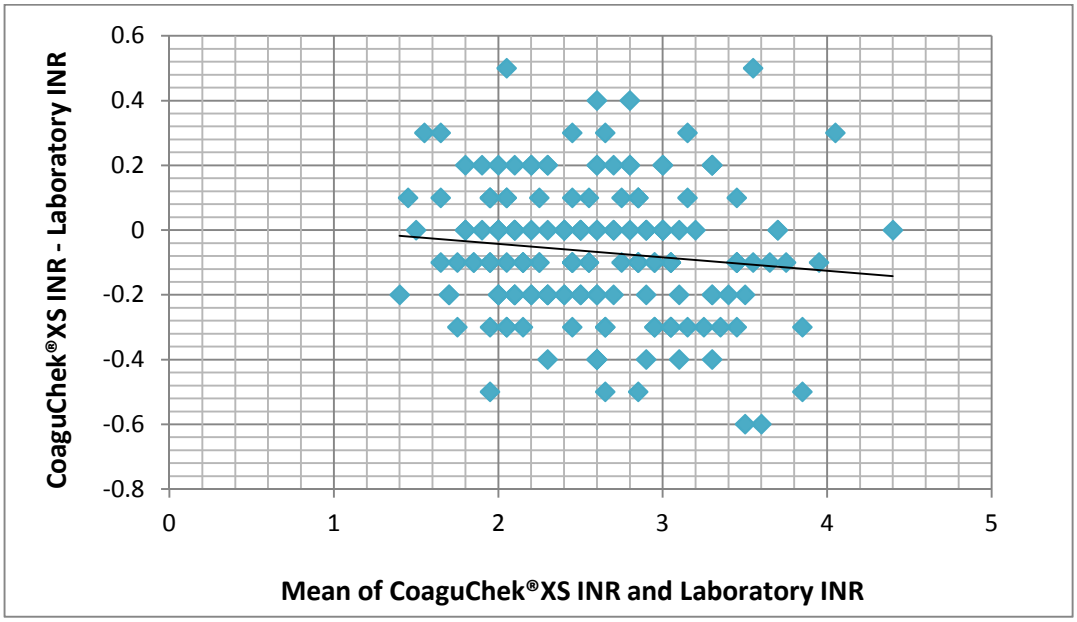


Figure 34: Bland-Altman style bias plot for CoaguChek®XS and laboratory INR values



6.4.1.6 Warfarin knowledge

Participants were awarded a warfarin knowledge score based on their responses to the OAK Test. A pass or fail grade was also awarded, with the pass mark being set at 72.4%. Repeated OAK Test responses were available for 35 participants. There were no significant differences found in the INR control of participants during the

intervention based on their baseline level of warfarin knowledge (p = 0.38). Table 30 shows the median scores (and ranges) of participants at baseline and at the conclusion of the intervention period.

Table 30: Warfarin knowledge scores during the study

Knowledge scores	Median (range)	*p*
Pre-self-monitoring	85.0 (35.0-100.0)	0.730
Conclusion of PSM period	80.0 (40.0-100.0)	

There was no significant difference shown in knowledge in the long-term follow-up group between baseline and the conclusion of the PSM period and training. The knowledge questionnaire was not repeated following the education session for all participants of the long-term follow-up group so was not analysed for this cohort.

During the Pharmacy-Based Model Enabling Patient Self-Monitoring of Warfarin project, changes in knowledge were evaluated both in the two to four week period following the education session and again at six months. These scores, based on the results of 22 patients, are shown in Table 31 and Figure 35.

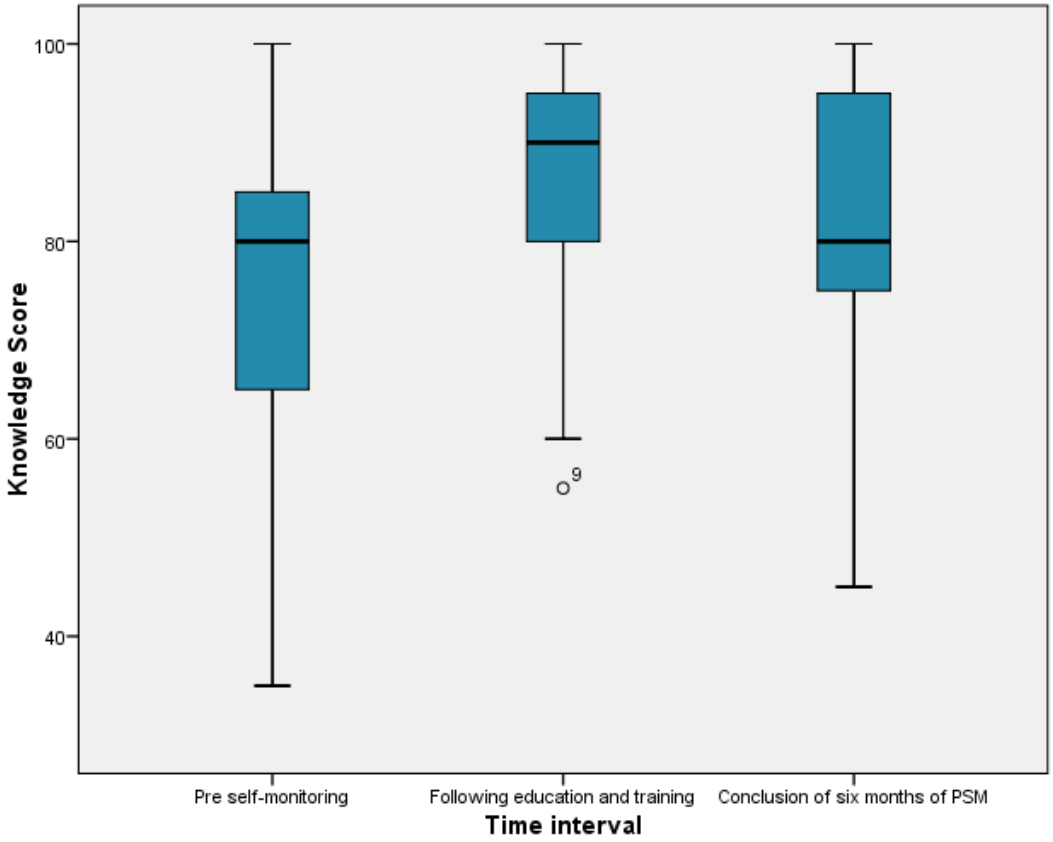
Table 31: Warfarin knowledge scores during the Pharmacy-Based Model Enabling Patient Self-Monitoring of Warfarin project

Knowledge scores	Median (range)	*p*
Pre-self-monitoring	80.0 (35.0-100.0)	} 0.01
Following education and training	90.0 (55.0-100.0)	} 0.36
Conclusion of six months of PSM	80.0 (45.0-100.0)	

Comparison of the test results at the three time intervals demonstrated a significant difference between the scores (X^2=8.716, df=2, p=0.01). Further investigation comparing pairs of tests demonstrated a significant increase in knowledge scores seen between those obtained prior to self-monitoring training and those obtained following education and training (Z=-2.86, n=22, p<0.001, two-sided).

Although the median warfarin knowledge score dropped between the post-education period and the conclusion of the PSM period, this fall was not statistically significant (p=0.36). While this is contrary to expectations when looking at the actual median scores, and the corresponding range of scores, it can be better explained by examining the spread of scores at each time interval (Figure 35). Despite the median falling by the end of the six months of PSM, the majority of the knowledge scores remained higher than they had been at baseline.

Figure 35: Distribution of knowledge scores over time



6.4.1.7 Quality of life

Participants completed the EQ-5D QOL questionnaire at baseline and on completion of the intervention phase, with median QOL utilities of 1.0 (range -0.2 to 1.0) and 0.8 (range 0.1 to 1.0). There were no significant changes in the quality of life of

participants, as measured using the EQ-5D instrument, during the self-monitoring period (p=0.202).

6.4.1.8 Clinical outcomes

One event of major bleeding and one of thromboembolism were observed during the intervention. One patient experienced an intracerebral haemorrhage which forced withdrawal from the study. Another experienced an ischaemic stroke requiring hospitalisation but not severe enough to necessitate withdrawal from the study. Both events occurred in the presence of a therapeutic INR.

There were two deaths during the intervention period due to unrelated causes (both acute myocardial infarctions - one related to alcoholic liver disease, the other secondary to multiple cardiovascular risk factors.). Again, both events occurred in the presence of a therapeutic INR.

6.4.1.9 Stakeholder satisfaction

Completed evaluation forms were received from 39 of the 40 (97.5%) patients who completed the long-term follow-up phase. They were also received from 17 of the 42 (40.4%) GPs and seven of the participating pharmacists. Participants were asked to rate their agreement with given statements out of ten, with 0 being strongly agree and 10 being strongly disagree. A summary of the responses to the evaluation questionnaires is shown in Table 32. A visual representation of the full set of responses to each of the questionnaires is shown in Appendix 28.

Table 32: Summary of evaluation responses

Question summary	Median score (range)		
	Patient	**GP**	**Pharmacist**
Valuable service	0.5(0.0–5.5)	2.0(0.0-8.0)	0.0(0.0-3.0)
Confidence in warfarin	0.5(0.0–7.5)	3.3(0.0–10.0)	1.0(0.0-3.0)
Feedback and training	0.5(0.0–3.5)	4.8(0.0-9.0)	1.0(0.0-4.0)
Confidence in accuracy of CoaguChek®XS	0.5(0.0–5.5)	1.0(0.0-9.0)	-
Ease of use of monitor	0.5(0.0–5.0)	-	-
Home monitoring preference	0.5(0.0–8.5)	-	-

6.4.1.9.1 Patient responses to self-monitoring

All feedback regarding the service was extremely positive, with median scores for almost every statement being 0.5 (with the highest possible rating being 0.0). Despite the results of the EQ-5D, patients did report that their overall quality of life had improved as a result of being able to monitor their warfarin therapy at home, awarding the statement a median score of 0.5 (range 0.0 – 6.5). Patients expressed a preference to monitoring their INR at home and found the CoaguChek®XS device simple to use and had confidence in its accuracy, with median scores of 0.5 (range 0.0 – 8.5), 0.5 (0.0 – 5.0) and 0.5 (0.0 – 5.0), respectively. Patients reported self-monitoring to be a valuable way of monitoring their therapy and found the initial training to be beneficial, including improving their warfarin knowledge, despite the results of the OAK Test. These statements received median scores of 0.5 (0.0 – 5.0), 0.5 (0.0 – 3.5) and 0.5 (0.0 – 6.5), respectively.

6.4.1.9.2 GP responses to self-monitoring

GPs believed that their patients found the self-monitoring method to be a worthwhile service and that their patients coped well with the model, with statements receiving median scores of 1.0 (range 0.0 – 8.0) and 1.5 (range 0.0 – 7.5), respectively. They felt that 5% to 100% (median of 50%) of people taking warfarin would benefit from this service. GPs were generally confident in the accuracy of the

CoaguChek®XS INR monitor, with the statement scoring a median of 1.0 (range 0.0 – 9.0).

6.4.1.9.3 Pharmacist responses to self-monitoring

Pharmacists felt that the self-monitoring service had a positive impact on their relationship with patients and that more patients could benefit from this service, with statements scoring a median of 2.0 (range 0.0 – 4.0) and 0.0 (range 0.0 – 1.0), respectively. They felt that 25% to 75% (median of 40%) of people taking warfarin would benefit from this model of care. Pharmacists felt that the self-monitoring model is a valuable service to patients, a feasible way to manage patients on warfarin and they felt confident about identifying patients who may be suitable for this model of care, with statements receiving median scores of 0.0 (range 0.0 – 3.0), 1.0 (range 0.0 –1.0), and 1.0 (range 0.0 – 3.0), respectively.

6.4.2 Exploration of Patient Views of Self-Monitoring of Warfarin

6.4.2.1 Participants

Interviews were conducted with 38 participants of the long-term follow-up PSM project. The participants were from Tasmania, South Australia and New South Wales and spread between rural, regional and metropolitan locations. The participants were a diverse group of people with ages ranging from 22 years through to 89 years, though the majority were aged 60 years and above. A small majority of participants were male. There was a mixture of employed and retired participants, however the majority were retired as would be expected given the median age of the subject group. Indications for warfarin were predominantly AF and mechanical heart valve insertion, however clotting disorders and venous thromboembolism were also indications for a number of participants. Some participants had other medical conditions which were likely to impact on their daily life, while others had only warfarin, and the condition for which they were taking warfarin, to manage. The demographics of the participants are shown in Table 33.

Table 33: Interview participant demographic details

Pseudonym	Sex	Age	Indication	Months of warfarin	Duration of PSM	Marital status	Employment status	State/Area
Alex	M	44	Mechanical Heart Valve	36	23.7	Married, with young kids	Works in IT	Tas Metro
Anna	F	78	Atrial fibrillation	6	10	Married	Retired	SA Metro
Bonnie	F	86	Atrial fibrillation	6	21.7	Widowed	Retired	Tas Metro
Connie	F	77	Atrial fibrillation	36	22.4	Alone	Retired	Tas Metro
Craig	M	80	Atrial fibrillation	96	7.8	Married	Retired	SA Metro
Damien	M	39	Venous Thrombosis/Cancer	6	9.8	Lives at home	Disability pension	SA Remote
Dave	M	89	Atrial fibrillation	6	19.8	Married	Retired	NSW Regional
Derek	M	71	Atrial fibrillation/Stroke	48	23.4	Married	Retired	Tas Metro
Gabby	F	22	Venous Thrombosis/Clotting disorder	6	5.1	Single, at home (Tom's daughter)	Student nurse	SA Metro
Gavin	M	65	Mechanical Heart Valve/Venous Thrombosis	312	24.5	Married, with kids 13yo - 42yo	Retired	Tas Rural
Gordon	M	85	Atrial fibrillation	6	8.9	Married	Retired GP	Tas Metro
Harold	M	80	Mechanical Heart Valve	60	24.9	Unsure, has a live-in companion	Retired	Tas Rural
Heather	F	56	Atrial fibrillation/Venous Thrombosis	168	5	Married	Disability pension	Tas Rural
Ian	M	79	Atrial fibrillation	60	22	Widowed during trial	Retired	Tas Metro
Jack	M	58	Mechanical Heart Valve	6	10	Married	Music store	Tas Metro
Jane	F	77	Atrial fibrillation	120	9.3	Widowed, but has a companion	Retired	SA Metro
Joe	M	66	Atrial fibrillation	36	22.9	Widowed, but has a companion	Retired	Tas Metro
Judith	F	61	Atrial fibrillation/Stroke	6	20.4	Married	Teacher, retiring	NSW Regional
Lachlan	M	70	Atrial fibrillation	172	20.4	Married	Retired	NSW Regional
Liz	F	81	Unknown	96	10	Widowed	Retired	Tas Metro
Mandy	F	69	Atrial fibrillation	6	20.5	Married	Retired	NSW Regional
Marge	F	76	Atrial fibrillation	72	9.5	Alone	Retired	Tas Rural
Mark	M	66	Mechanical heart surgery/problems	420	9.4	Married	Employed	Tas Metro
Mathew	M	76	Venous Thrombosis	6	9.4	Married	Retired	SA Metro
Narelle	F	61	Atrial fibrillation/clotting disorder	138	20.6	Married	Self-employed	Tas Metro
Olive	F	72	Atrial fibrillation	108	21.5	Widowed during trial	Retired	Tas Metro
Paul	M	61	Venous Thrombosis	48	9	Single	Disability pension	Tas Rural

Pseudonym	Sex	Age	Indication	Months of warfarin	Duration of PSM	Marital status	Employment status	State/Area
Peter	M	73	Atrial fibrillation/Stroke	72	23.4	Married	Retired	Tas Rural
Robyn	F	41	Venous Thrombosis/Clotting disorder	6	9.1	Single	Disability pension	SA Rural
Rosemary	F	55	Atrial fibrillation	180	20	Married	Medical admin	NSW Regional
Ross	M	56	Mechanical Heart Valve	46	3.5	Married	Self-employed	Tas Remote
Sally	F	44	Venous Thrombosis/Clotting disorder	18	9.1	Married, with young kids	Nurse	Tas Metro
Steve	M	55	Atrial fibrillation	2	5.6	Married	Builder	Tas Metro
Terry	M	54	Congenital heart defect/Stroke	18	22.9	Married, with young kids	School teacher	Tas Metro
Tim	M	73	Atrial fibrillation	120	23.2	Married	Retired	Tas Rural
Tom	M	54	Venous Thrombosis	1	2.7	Married, with kids (Gabby's father)	Financial planner	SA Metro
Wendy	F	63	Atrial fibrillation	204	9.5	Married	Retired	Tas Metro
William	M	80	Atrial fibrillation	96	22.8	Widowed	Retired	Tas Metro

6.4.2.2 Introduction to findings

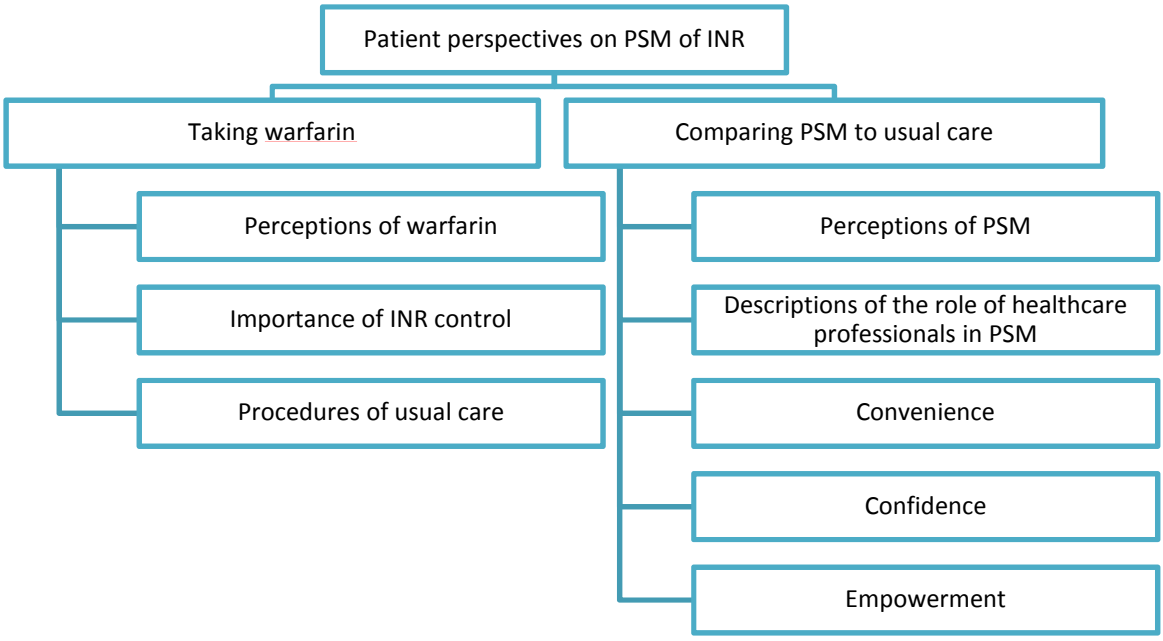
As described in the methods above, the codes identified during the analysis process were grouped within eight overarching themes:

> *Confidence; Convenience; Descriptions of PSM; Empowerment; Healthcare professionals; INR control; Perceptions of warfarin;*

These themes were then amalgamated under higher level themes of 'Taking warfarin', to describe what taking warfarin was like prior to self-monitoring, and 'Comparing PSM to usual care', to describe what and how things had changed with self-monitoring. The resulting structure of the themes and sub-themes is shown in Figure 36.

The following results are split into two sections - one discussing the descriptions that participants gave of taking warfarin, the other their comparisons of PSM to usual care. Under each section, the corresponding themes are discussed in detail. Each subheading represents a theme. Under each subheading the nature of the patient accounts relating to each theme, and its corresponding codes, is described, drawing heavily on examples from taken from the interviews.

Figure 36: Structure of themes and sub-themes



6.4.2.3 Social and background factors impacting on themes

It is increasingly recognised in the sociological literature that social factors impact on a person's experience of living with a chronic illness. These social factors include age, gender, and social class and social ties.[395, 396] Increasing age, and the corresponding stage in the life cycle, are suggested to increase people's acceptance of illness as part of the normal ageing process.[397] Gender is also proposed to play an important role in experiences of health. It has been suggested that women are more likely than men to report ill health and symptoms of concern.[398] Social status, including education and income in particular, has been shown to contribute to health behaviours,[399, 400] while social ties, such as close personal relationships and marriage, have also been shown to be important in reducing the perceived burden of chronic illness.[401]

Emerging themes from the data in this study were explored to identify any similarities and differences in perceptions that may have been apparent between participants and attributable to differing social factors, as described above. Despite

the expectation that some of these social factors may have impacted on participants' experiences of living with a chronic illness, and hence on their perceptions of the convenience, confidence or empowerment associated with PSM, clear differences did not emerge from the interview data.

6.4.2.4 Taking warfarin

The experience of taking warfarin is something which is not taken lightly. Many participants spoke about the impact it had on their lives. Some participants discussed the emotional impact of taking warfarin. They expressed uncertainty about knowing whether what they were experiencing was normal or related to poorly controlled warfarin therapy. For one participant in particular this uncertainty translated into episodes of considerable anxiety. Others were more relaxed about warfarin, sometimes to the point of being at the opposite extreme, and expressed little concern about their therapy.

Some participants discussed other areas of their lives that were affected by taking warfarin and the subsequent need for regular INR monitoring. Aspects that were discussed included the impact on their ability to travel, the perceived need to change their diet or modify their intake of other medications, and the impact on other medical procedures. Warfarin's demand for tight INR control and its extensive list of interacting substances were discussed both in terms of inconvenience and reduced confidence.

6.4.2.4.1 Perceptions of warfarin

Many words were used by participants throughout the interviews to describe warfarin. Most descriptions were negative and laced with perceptions of fear or danger. For example, "rat poison"(Liz), "arsenic"(Wendy), "it's a killer"(Craig), and "heck of a weight on my shoulders"(Ian). However, some participants were more comfortable with warfarin and recognised its positive aspects in preventing

unwanted events. For example, Narelle stated "it has been a lifesaver for me." They also discussed the impact of concomitant illnesses on their feelings of taking warfarin.

The reasons for feeling negatively about warfarin often appeared to stem from a fear of side effects. Bleeding side effects were of concern to many, particularly as there is no way of knowing the INR, and consequently the increased risk of bleeding, without having a test. The inability to know whether any bleeding that occurred was simply due to an injury or due to a high INR was also raised:

> *I was worried when I had this accident because the bruising was substantial and I wouldn't have had as much bruising, and I got several haematomas, some on my ribs and a huge one on my leg and one on my head still… that's the only downside with warfarin, if you injure yourself you do bleed a lot. (Olive)*

> *You might wake up in the morning, get up, get dressed and you no sooner start to have breakfast and your nose will start to bleed and you don't know what you should do. Panic. Ring and try to get an appointment with your doctor. Oh yes, next week, you know, you can't get in straight away… Have the blood taken and I might have missed the [pathology collection] run, that worries me. The results would be back with the doctor in the afternoon, quite often the doctor wouldn't give you the results that afternoon and I might have had a blood nose in the morning. (Ian)*

This fear of side effects was something which could have been allayed by explanations given by health professionals at the commencement of therapy. Instead, the explanations received by many participants were raised as points of concern:

> *I didn't get a great deal of education, because I ended up going, I went to the GP who sent me off to have a scan, back to the GP, and then… the nurse sent me straight to hospital, I didn't even see a GP when I went back there, straight into hospital, where they threw Clexane and warfarin at me and said you have a blood clot and then basically left. (Gabby)*

> *[the doctor] said nothing, you know, just if you are not on warfarin and you don't monitor it, I think he said to me you are 20 times more likely to have a repeat… and he said it will be just, one day it is just like crossing the double white lines, you will have a stroke and you know, you'll be gone, and I said, oh, right. (Terry)*

A few participants expressed a more positive, inclusive experience with the initial warfarin education and interestingly they were some of the few who did not express a fear of taking warfarin:

> *…my acceptance of warfarin is… explained by the fact that [the cardiologist] said that I have got this atrial fibrillation… I didn't have any physical symptoms… [he said] the concern is you are five times more likely to have a stroke than the normal population that doesn't have atrial fibrillation… so I am going to prescribe you warfarin. And I said, what, rat poison? He said, yeah the same stuff, he said, it's a very good drug, it is cheap and very effective, but he went through all the basic problems, etcetera. So I said, right, so really I am just taking it as a preventative? He said, yeah, that's all. Right, that's fine , how long do I have to take it? He said, probably the rest of your life. I said, okey doke. (Tim)*

Despite, the fear of warfarin expressed by many participants, there was a strong preference for taking warfarin, regardless of its risks, to prevent thrombotic sequelae such as strokes. This is probably not surprising as those who decide that the risks of warfarin outweigh the benefits are unlikely to persist with treatment

and as such would not have had the opportunity to participate in this study. Some patients held this belief despite not having previous experience with thrombotic events. Lachlan felt "…it is better to be sure than sorry, I think this warfarin, well, you know, I think it does help me I think, so you know I am better off on it than off it, and it is not worth the risk of having a clot in the heart is it…" While Anna described her decision as "…the nurse and doctor said I have to take the warfarin in case of stroke, and at first I didn't really want to, I mean it is rat poison isn't it, but then the stroke is a lot worse and I thought, yeah, better…" Other participants had previous experience with thrombotic events, and this translated to an increased anxiety to avoid future events and to monitor the INR closely. Narelle was one participant who had previously had a stroke, she said "I am really quite paranoid about clots having had two. They are devastating things to have, I mean a stroke is, I was paralysed."

For most participants, having a concomitant illness impacted negatively on their perceptions of taking warfarin or contributed to their anxiety. Other conditions added to stress related to the potential for poorer INR control and poorer outcomes, the added burden of appointments, keeping on top of other symptoms and a general reduction in confidence. One participant described his wife having Motor Neurone Disease and his role as her primary carer as contributing greatly to his anxiety of taking warfarin:

> *…you can become frightened, and being, having anxiety, which is slowly getting better now because [my wife] has finally gone, and it was probably worry, that I cark it before she do, the matter of I wanted to see her out and who would expect that – 19 years for a three and a half year average disease, nobody… it's a worry when you've got something on, you don't want to let something that can be attended disappear and knock you out before you need to go. (Ian)*

Only one participant described their concomitant illness as having perhaps a positive impact on their feelings of taking warfarin and the procedures involved. Rosemary was on long term dialysis and as such had had a lot of exposure to needles and did not find the blood tests themselves to be a negative of taking warfarin.

6.4.2.4.2 Importance of INR control

Interlaced with discussions of the side effects of warfarin were discussions on perceptions of the importance of INR control. Some participants discussed their doctor's advice on what INR levels they needed to be concerned about. In some instances participants expressed this in terms of providing peace of mind that INR readings need not be as strict as they first believed. Gordon, a retired GP, expressed his view on INR control "…some doctors are very fussy about maintaining a strict range, and alter a dose every week. I am more lax, if it is 1.8 or 3.2 I don't worry." Robyn also described her experience:

> *It's really odd, because when you first go on [warfarin], they have this whole education on your INR levels and you know they want you between 2 and 3 and they pretty well to start with make it sound like well if goes below or above that, then we have got issues, you know. And now it's like my doctor says well if it's 1.6 I am happy with 1.6 to 4, you know, we would like you therapeutically to be between 2 and 3, but we're not going to get up in arms if you are at 1.6 or 4. It's when you go below 1.6 or start going above 4. He said, we don't like it at 4, but we have people come in with INRs of 10, you know, and we just deal with it at the time. Having a day at 4 is not going to be something that's going to cause any detrimental problem, as long as we get on top of it and bring it back down, so over a period of time it must be between 2 and 3.*

Some participants discussed their difficulties in maintaining steady INR control as their INR fluctuated considerably within small periods of time and whilst on the

same dose. This translated to a need to attend usual care sites frequently, in some instances as often as multiple times per week. Gavin has a lot of issues with the functioning of his bowels and described huge degrees of variation in his INR levels with no apparent change in diet or medications. Others, such as Mark, frequently participated in activities which cause their INR to fluctuate:

> *…[the INR] does tend to fly out with picking up a bug, changing diet is more like travelling, but just being home, if I pick up a bug and with long term warfarin, it cuts down the, I find, cuts down the resistance for picking up stuff, so I tend to pick up whatever is the going thing and it means … going off to pathology day after day, or every two days…*

Others, like Rosemary, described very steady INRs with little or no variation over the course of time.

The importance of maintaining good INR control for most participants related to the desire to prevent thrombotic events and minimise the chances of bleeding. Peter had a much more sombre opinion on the importance of maintaining a strict INR after having experienced a stroke whilst within the therapeutic range. Interestingly two participants expressed a complacency relating to regular testing and maintaining therapeutic INR control. They did not perceive good INR control as a matter of life or death, despite being aware that over or under anticoagulation could indeed result in death and one of these participants having experienced a number of thrombotic events in the past:

> *I am a bugger for going over and having my INR done at the best of times, I tend not to take it too serious, which is probably silly… I mean if it were a life and death type thing, then I would… Well I would be ringing up and saying look, enough is enough you know, I have had enough of this, what am I doing wrong you know, I am not eating anything different, I don't drink, don't smoke, so and*

> *he said it is just the way it is, sometimes. He said, you will need to have another one now and another in three days' time, so back over there again, so in the end I just get a bit complacent about it and don't bother. I feel what I don't know doesn't hurt me, so, which is a bit naughty, but you know. And you know, I say well it is not life threatening but yeah, sometimes it could be… I just get slack on it, you know, and I should be concerned because it changes for no reason you know… (Heather)*

In stark contrast Terry, who had previously experienced an ischaemic stroke, held the importance of INR control above everything else. His opinion was that regardless of anything else, if his INR was poorly controlled he could die. His opinion was so strong that he was reluctant to take medication prescribed following a diagnosis of lymphoma in case it interfered with his INR control:

> *…the specialist said, oh, you have got lymphoma, and I went, what, are you sure, and yes, she went to pick up the phone and said this is all typical of blah, blah, blah, blah, blah. And I want you on this medication. And it was because I was on the INR, I said no, stop, stop, stop… and I said no, just hang on a second. How will that affect my other medication?*

6.4.2.4.3 Procedures of usual care

The practices that constituted usual care in terms of INR testing for each of the participants varied considerably. For some, usual care involved a healthcare professional coming to the participant's house to obtain a blood sample. For others, it involved attending a pathology clinic or doctor's surgery to have the blood sample taken. In some instances usual care involved the use of a POC device, like that used in the study, while in most it involved the traditional venous sample method. For some participants usual care comprised a combination of both. The usual care procedure was likely to impact on perceptions of the convenience of taking warfarin.

Sally described her usual care procedure as "…a monthly duck into the pathology and every time you go to pathology you always pick the wrong times to, it is full of people and then I forget to ring the doctors to get my results…" Judith, a teacher in regional NSW, described her experience as:

> *Make an appointment, go and see the, usually a practice nurse actually, the surgeries I go to have practice nurses, they would do the INR with one of the little machines and then we would wait until they could attract the attention of the doctor in between patients to make sure he knows, so that could take an hour maybe and then I'd drive home. And at some stage I was actually having to go and have blood taken, it must have been earlier in the piece, at the path lab, so that was, and that was an issue because I have very fine veins and you know, sort of three holes later they might have got enough blood to do the INR test.*

Disadvantages of the usual care procedure were discussed by many participants. Venesection was described as a problem by some participants due to poor venous access. For others it was the fact that they had been on warfarin for so long and had had so many blood tests that they now had scarring of the vessels usually used to obtain venous samples:

> *I have had [blood] taken out of my feet and you know all sorts. In my hand once and the doctor held my leg down and he is going pump, pump, and he was literally pumping out of my hand… you know sometimes it takes so long to get a small amount of blood out of me, you know that, you know, when it goes to the lab that they are going to say sorry, it has already started to coagulate, you know before it reaches the bottle, going through the tubing it is coagulating, so… And I have been called back in to get, back into the surgery to get the blood taken again because the first attempt was a failed attempt. (Robyn)*

> *The end result was that my veins are scarred to blazes and so for that reason they try to lessen the venisections. The most recent venisection was last Tuesday and that is a very good result [shows a large bruise]… There are times when they have had three tries and then given up. Different nurses have different capabilities. I feel a bit silly when I go to [pathology] and say to one of the girls, 'now please, I want you to use the fine needle' – who are you to tell me what my job is? Then I have to go through the process of explaining. (Mathew)*

Some participants expressed transporting themselves to the usual care site as a barrier, either due to the distance to the usual care site or an inability to drive themselves. In cases where participants were reliant on family members to attend usual care sites this added an additional barrier. For some participants the fact that they had to transport themselves to the testing site translated to a poorer level of compliance with testing. Derek now relies upon his wife to get to a testing site "… I've taken myself off driving because I can't, I shouldn't drive. It's not that I can't drive, I shouldn't drive when I'm a risk to other people as well as myself…" Heather also relies on her family to assist with transport "I don't have a license now because they, at the moment I have lost it for medical reasons, hoping to get it back, so it's really hard for me to get over [to pathology]."

Another issue that was raised as a concern of usual care by some participants who had venous samples taken was the time taken to get the INR result back and subsequent dosage adjustment advice from the GP. This delay caused some participants considerable anxiety, especially where the result was not returned until the following day:

> *[the doctors] have got one of these machines, but before that, that had to go and be read or whatever they do to it and then come back to the doctor and it would be another couple of days and if the doctor was busy, sometimes a week, from*

> *the test until you got the results. What I am trying to say, if you had a high reading, you could be in trouble, or a low reading even, the same thing, and in that week in between you can get into a lot of trouble, believe me. (Craig)*

> *…the trouble is if you do it with pathology you got to ring up after three o'clock the next day. And when you do ring up they say 'we're very busy'… See, when I first went on to that business, I was told I had to get it done, when they put me on warfarin, it had to be done in the morning and I had to ring up that night… Well look what you gotta do now, you gotta wait until the next day, and that is a worry to you when you have to wait. As I say, they say ring up after three o'clock and you ring up and they say we're busy at the moment, you have to wait until three o'clock the next day, that's no good, you can't do it that way. As I said, that worries me is when that [cardiologist] said it's got to be done, you know, and they change it, see. (Harold)*

Interestingly, Heather discussed her poor compliance with usual care in terms of a feeling of guilt associated with being able to access pathology testing for free. She was financially dependent on a disability pension and had a desire to contribute something towards the cost of her healthcare as she felt herself a burden on government services. The fact that she was being bulk billed actually deterred her from accessing pathology testing.

6.4.2.5 Comparing self-monitoring to usual care

The experience of performing self-monitoring was discussed by many participants in terms of comparing it to their usual care procedure. Comparisons were made on the basis of effects on confidence, both in terms of taking warfarin and in the reliability of INR results. Convenience of the two procedures was compared, including discussions on the cost comparison for each model of care. Participants

also described feelings of empowerment that were exclusive to PSM when compared to usual care.

6.4.2.5.1 Perceptions of self-monitoring

Words and phrases used to describe PSM were overwhelmingly positive and indicated high levels of satisfaction with the monitoring procedure. For example, "best thing since the wheel" (Craig), "it has been a positive boom" (Gordon), "unqualified success" (Mark), "changed my life" (Ian), and "very handy" (Bonnie). Through these words participants expressed their passion for PSM and gave the sense that PSM had reduced their levels of anxiety relating to warfarin. It was described as something of value which freed them to get on with their lives. Some went as far as to describe PSM as lifesaving, while one described being reliant on PSM and not being able to do without it.

Many participants also described PSM in comparison to blood sugar level (BSL) testing. BSL testing is usually performed by people with diabetes to enable them to monitor their sugar levels and self-adjust their dose of insulin if necessary. It is a test which also uses a portable device and a finger prick blood sample, but one which is currently more widely used and accepted than POC INR testing. Comparisons included the process being no harder than BSL testing and similarities between the testing procedures. Jane described her familiarity with the testing process arising from caring for her husband in the past, "There weren't any problems to me, because when my husband was dying he developed diabetes and I was used to helping him prick his finger and use the diabetic machine, similar kind of thing". Many participants also commented on the widespread use of BSL testing and its benefits, and their inability to comprehend why INR testing is different and is not supported by government subsidies:

> *I guess with personal preference some of the drugs they have got on the PBS for some things I find it, especially for things like blood sugar testing for diabetics, I find it strange that they have that and not this and personally disappointing. I would like to see that changed because I think it makes sense. (Alex)*

> *To me it is on par with your blood sugar and diabetes, and that is becoming more simple isn't it, they are inventing and devising simpler ways of doing it for blood sugar and everything so it is the same thing. I mean you are only pricking a bit of blood and analysing it, so okay, it is a different strip and it is analysing a different thing, the INR, but to me it should be more widespread, you know. (Mandy)*

The language choices of the participants convey the confidence, convenience and empowerment they associate with PSM. These opinions of PSM seem in many cases to be independent of the support offered by their treating healthcare professionals.

6.4.2.5.2 Descriptions of the role of healthcare professionals in self-monitoring

Most descriptions of healthcare professionals attitudes towards PSM related to the GPs involved in their care. The support of the GP for PSM was initially required for participation in the projects. However, a small number of GPs who had consented to their patient participating subsequently offered little support or were reluctant to rely on the POC results. Support of GPs appeared to be very dependent on the individual GP themselves. Mandy was supported by her original GP throughout the trial but this GP left the practice in the months leading up to the interview. The doctors remaining at the practice were unwilling to support her continuing with PSM and she was considering changing practices to ensure she could continue self-monitoring. Conversely, Tim found he got more support when his original GP left the practice:

> *[my first GP] didn't like it because I would do what I do with [my current GP]. I would change my dosage, very minor, and tell him afterwards. On a couple of occasions he said I am supposed to be the doctor here… initially I used to say to him look, I get my INR testing and, for argument's sake, it would come back 1.9 for example, and I would say, look, should I increase my dose by perhaps 1mg, and he would say either yes, or say no go up half a mg… I think that's why [my current GP's] quite happy to go along with, basically I am diagnosing myself, but that is based on, I have been taking it since 1996… (Tim)*

Most participants reported positive feedback from their GPs and described high levels of support. They described their GP feeling PSM had had positive effects, in terms of improved patient knowledge and the GP's peace of mind. Some GPs were happy to hand the responsibility of INR monitoring and minor dose adjustment to the patient, though it was acknowledged that even the supportive GPs did not consider PSM as suited to all patients:

> *I said to my doctor, what about the fee that you charge when I come to see you. She said it is nothing about the fee, it is the amount of time that I save through being able to do it. She is in love with it too. She reckons it is marvellous. She said I wish I had a thousand of them to dish out. (Craig)*

> *[my doctor], she's very much in favour of this. Whereas [my late husband's] doctor wasn't, he didn't believe in it. How silly, I mean it is really good. [my doctor] is happy with me keeping going with this, she knows I will get in touch if there is anything not right… (Olive, whose husband had also taken warfarin)*

> *He is certainly not disappointed that I have got my own, I mean it is neither here nor there with him, he is a very popular doctor and he is hard to get in to, so he has more than enough on his plate without me pestering him… he made it plain that you know, like there is quite a few of his patients that he wouldn't like to see*

> *have their own, because he wouldn't be confident of their ability to use it properly and/or interpret the results properly, but he must think that I have half a brain. (Ross)*

Two participants raised other medical specialists, one commenting on the support offered by their cardiologist, while another found their gastroenterologist was not happy to rely on the POC results. This difference could possibly reflect a difference in education and understanding of the POC INR technology.

Despite being raised during the interviews, and the PSM training being delivered by pharmacists, the role of pharmacists in PSM was not discussed in detail by participants. Two participants spoke of their good relationship with their pharmacist and their pharmacist's interest in PSM. However, most discussions about pharmacists tended to centre on their role in the provision of consumables such as test strips. Participants generally seemed to view their warfarin care as something that was managed solely by their doctor or by themselves in collaboration with their doctor. There was little recognition amongst participants of the role pharmacists could play in managing warfarin therapy. This may be because it is not currently a standard model of care and as such is not one which participants had ever considered, or it may be that participants do not feel there is a role for pharmacists in warfarin management and that it should remain the domain of doctors. These interviews did not delve deeply enough into this issue to draw any conclusions on the views of participants on a role for pharmacists in warfarin management. However, Gordon, the retired GP, did discuss other projects that were being undertaken by the research team and expressed support for a role for pharmacists in INR testing, suggesting that perhaps there may be support for a role for pharmacists in warfarin care:

> *That's probably a very good idea in that area where it's a bit selfish for one person to have one machine, where you can have people coming in, the pharmacist doing the test and one machine for a dozen people then that's much better distribution of assets. (Gordon)*

6.4.2.5.3 Convenience

Convenience associated with PSM emerged strongly with elements of convenience being discussed by all participants. Perceptions of convenience related to differences between PSM and usual care, in terms of testing procedure and site, impact of the testing method on other activities and the affordability of each model.

The distance to the usual care site was raised as a barrier to usual care by some. For a few this involved distances of up to 100km, while for others the distance was as small as travelling to another suburb. Even short distances were perceived as inconvenient. Rosemary's view was "basically, I am lazy, I don't like driving to appointments, so I would rather anything I can do myself is, suits me far better out here because everything is such a distance". Travel to the usual care site was also a barrier for people who had difficulty transporting themselves. Some participants were unable to drive for medical reasons and relied on their spouse or children to transport them or on taxis. Dave was nearly 90 and his daughter usually drove him to the doctor. When asked about her views on PSM, she stated "I thought it was great, because it saved me coming up and picking Dad up, taking him down to the surgery, then bringing him home again, so it worked really well for me". Other participants had difficulties on account of physical problems, including Craig, who suffered shortness of breath on exertion, Robyn and Paul, who were confined to wheelchairs and Tom, who had mobility issues following a broken leg. Liz, who was able to drive, raised the issue of having difficulties as she had to walk a considerable distance to the pathology collection centre after parking the car. Jane, a retiree from

Adelaide who had many adult children working in medical professions, expressed an alternative view and emphasised that she did not find usual care inconvenient as she enjoyed driving and attending her GP for INR testing. She was quite defensive of her independence and seemed to perceive being in support of PSM to be indicative of a reduced ability to care for herself. However, she did suggest that other people might find it convenient:

> *But like I say, it's really more I felt that people don't or have access to transport, maybe don't drive and a lot of people my age don't drive, and then it would be very useful for them. (Jane)*

Related to the convenience associated with not having to travel to the usual care site was the convenience of being able to do an INR test on the spot. While this obviously translates to not having to travel to usual care, participants expressed a satisfaction with being able to do it themselves at home at a time that suited them, not having to make an appointment, and not having to get changed to go out. Many people used the term 'easy' or 'easier' to describe being able to do the test themselves. Paul said "it makes it much easier to be able to do it on the spur of the moment when I think it needs to be done". His view was echoed by Damien who felt "it makes it a lot easier for you, you do not have to stop doing other things when you can go to the machine at a certain time and put your finger to the side of it and give them the blood and it tells you what it is meant to be". Bonnie's son was a pharmacist and performed her testing for her, saving her trips to pathology. She said "…it is always easier to do things at home…[my son] doesn't forget, you know, so he'll say it must be nearly time for you to look at your blood mum. And he will come and do it."

Practically, performing the test on the spot also translated to an instantaneous result. Participants discussed the uncertainty and inconvenience associated with

the delay in obtaining results with usual care. This was particularly evident when discussing interruptions to therapy. Dental extractions and hospitalisations were the reasons raised for interruptions to therapy. The convenience of PSM for these people stemmed from their ability to check their INR prior to and following the event, and in many cases to self-adjust their dose until achieving the desired INR. This was seen as particularly important in light of the current difficulties getting into doctors at short notice, such as following discharge from hospital:

> *Quite often I have been sent home from hospital without knowing what the INR was, a little note on the bottom of the discharge paper – see your doctor in three days' time. I think in that particular case it was 10 days before I got to see her. Your INR could be doing anything in that time… I came out of hospital with a reading of 1.6 and that is just not good enough. So I have had to use the [monitor] to basically get it up to where it should be… (Craig)*

In addition to having a positive effect during interruptions to treatment, PSM was also seen to have a positive effect on minimising warfarin's impact on other activities. For some this was closely linked to performing the INR test on the spot and not having to interrupt the activities of their day, including work, especially during periods when they required testing multiple times per week. Dave thought it was good having the test performed at home because "I haven't got to put my dinner suit on to go to the doctor". Mathew, who required considerable medical care for other conditions, was of the view that "you might say that it can't be too difficult when you are retired but you get all sorts of appointments… My wife needs assistance around the place. The less appointments outside the house the better, so I do find it beneficial… They all get fairly tiresome all these tests…". For others, it was the convenience of being able to travel without having to seek out a GP or pathology laboratory to have their INR tested. Many people raised this in relation to

overseas travel. However, the benefits for domestic travel were also recognised. Alex told of how he regularly travels interstate for work and described the benefits of PSM in his situation. Steve said "we are heading off shortly actually, I normally take the machine with me and test it while I am away… Saves running to the blood places to get tested all the time, you can test it yourself and if I find it too high I just give the doctor a ring and he tells me what to do".

Being able to test the INR using a finger prick blood sample was seen as a huge benefit to a number of participants. Participants relayed the adverse effects they had experienced with usual care involving venous sampling. For some it was a matter of displaying large bruises after venisection. Others, who had been on warfarin long-term, described a scarring of their blood vessels and a subsequent desire to preserve their venous access in case of serious medical events in the future. Tom, a middle-aged man from Adelaide, expressed a phobia of needles and a preference for his INR to be tested by his wife (who was a nurse) via finger prick at home:

> *I hate the bloody things [needles]. No, I don't know what it is, I have always, you know, I used to give blood and lay there, and they said stop coming back you keep falling over on us. Too heavy to catch, but ah, I don't know. But with those things it just goes into your fingers sort of thing, I don't have to look at it, [my wife] just does it and I end up with a sore finger, that's all… I'd miss half my appointments if I had to get in the car and do that sort of thing. (Tom)*

> *See, with [my GP], it's a problem, and when I went last time to [the local pathology], I didn't want to go to [the one on the other side of the city], oh, she said, here comes trouble. Now they can't get blood out of me, you know before there was two sisters, both tried and couldn't get any out of me, so with a finger prick at least there comes blood out. (Connie)*

Tom's needle phobia impacted on his compliance with usual care. A few other participants expressed a similar poor compliance with attending pathology for INR testing and suggested they tested more regularly when doing PSM. However, Paul, who has undergone a bilateral below knee amputation, felt that having his INR tested was important enough for him to maintain compliance whatever the process and not feel inconvenienced by usual care.

One aspect that is likely to impact on people's compliance with PSM outside of trial conditions is the perceived affordability of this model of care. The issue of affordability arose during many interviews. Some respondents were concerned about the ongoing affordability of PSM to themselves, while others discussed potential affordability issues to do with the health system as a whole.

The ongoing affordability of PSM to the participants was often discussed and a range of points of view emerged from these discussions. Opinions on the ability to pay for the test strips did not always reflect the socioeconomic status of the participant or their apparent level of education. Factors which appear to have impacted on participants' willingness to pay included their doctors' acceptance of PSM, the degree of concern they held about the adverse effects experienced with usual care procedures, and previous experience with thrombotic events. The impact of usual care on other activities and the participant's satisfaction and perceived benefits of PSM also influenced their willingness to pay.

INR test strips are not currently subsidised by the government through the PBS, or by other means such as is the case for blood glucose testing strips through the National Diabetes Services Scheme. As INR tests performed through pathology services are generally bulk billed most people have no out of pocket expenses for having the test performed. During the research project the materials required to perform self-monitoring were provided by the research team. Outside of the trial

participants would be faced with the ongoing cost of consumables, primarily the cost of the test strips for the monitoring device.

Many participants were retired or on pensions and some genuinely could not afford to pay for the test strips, or could not see a way of putting the strips in their budget, despite a desire to do so. Others could not see why they would make a financial outlay for test strips when they could have their INR tested at pathology at no financial cost to themselves. The expense of PSM to the participant was of particular concern to those who had considered the extra cost of making errors and wasting consumables:

> *…the strips are a little bit expensive because sometimes I have made mistakes, I mean I would prick and then the blood wouldn't come and then somehow I have got it wrong, and error, and then I have wasted a strip. (Anna)*

> *I swapped away from doing it myself because of the cost. And I can go to [pathology], the so called "experts", and it costs me nothing. So it seemed to defeat the purpose in a way… It wasn't economically sound because I mean I'm on a fixed income now, like being retired, and it all adds up. (Derek)*

When discussing the health system, three main points emerged. These related to the potential cost saving to the government, a reduction of pressure on an already stretched health system and a comparison to BSL testing by people with diabetes.

The cost of providing people with test strips, for example on the PBS, was recognised. However, respondents felt there would be an overall saving when compared to the perceived cost of pathology INR testing and GP visits to Medicare. Comparisons were drawn to BSL testing by people with diabetes and a few respondents commented on the available subsidies for BSL testing strips on the PBS:

> *…it would be great if they do put it on the PBS and it's got to save them money, I can't see how it couldn't, it's taking up person's time in [pathology], then it has to go to a lab, it's got to be transported and then the results, so it must be time consuming, whereas bang bang and I'm done, you know, in a few seconds it's done, so it makes perfect sense to me. (Gavin)*

> *It seems such a simple thing. I just wish someone could convince the government, it would save a fortune, honestly it would. Sure the machines cost $1000 each but compared to what Medicare has to pay and that, you know, if you mount it up… (Craig)*

> *I am surprised they haven't done this, because it is very expensive [for pathology] to do tests all the time for people as well. It must be more expensive than providing people with strips, surely. (Narelle)*

They also recognised that health services, particularly GPs, are already quite stretched and saw PSM as a way to reduce some of the workload of GP and pathology services. The GP shortage was raised as something which could be assisted by PSM as some perceived INR monitoring as something which need not require a GP visit, especially if the visit is simply to obtain a pathology request form:

> *…it also takes the pressure off the GP, you're not forever on their doorstep, you know, or pathology… just taking the pressure off the system a bit by doing it yourself, it is really important… Less people coming to the surgery that don't need to, just for a bit of paper… (Jack)*

> *The government as a whole needs to look at that because if they were sensible about it, they would fund the strips because it is cheaper for them. And the doctors will be happier because they're not cluttering, there is a GP shortage, so there is all this time taken up with something that doesn't need to be done at a*

GP level, and costs us more than letting people do it themselves, which is quite feasible, so, you know, that's introducing logic into the equation. (Alex)

6.4.2.5.4 Confidence

Confidence associated with PSM also emerged strongly with elements of confidence being discussed by almost all participants. Responses suggest that there is a perception of increased confidence with warfarin therapy associated with PSM and being able to check if the INR is out of the target range. PSM also came through as improving confidence through decreasing feelings of uncertainty and anxiety. Participants expressed confidence in the accuracy of the POC devices and a satisfaction with the reassurance having the POC device provided.

PSM gave participants the ability to check if their INR was out of range at any time that suited them. This was important for some participants as they placed a lot of importance on knowing that their INR is within range simply because they are aware of what it should be and like to keep an eye on it. They felt this gave them the opportunity to see a doctor if they needed to, without waiting for their next appointment. For others, there were times when they wanted to check their INR as they suspected something may be amiss, for example if they were feeling unwell or experiencing suspected over-anticoagulation:

Well, I can take it at home and ring up and tell [the GP]. See we had a problem here once, but what I did, accidentally took an overdose, and one evening I thought, did I take it, and I got a container for every day, but sometimes I put two lots in for two weeks, and so I didn't, did I take it, no you didn't, did you take it, no you didn't. So I took it again and that is when it went 4.2 and 4.3 the same day. (Connie)

I do a lot of woodwork and that, and fairly regularly cut myself on a chisel or something… You know, and sometimes things take longer to stop bleeding, and

> *you think, ooh, I wonder if that is because of the cut or because my INR is really high at the moment. I can just do a test and it gives you that confidence. (Alex)*

PSM also gave people the opportunity to monitor possible interactions with warfarin. Many people raised the importance of being able to check their INR if their diet was significantly altered, particularly for those who grow their own vegetables and have a diet that changes with the seasons. Ross was one such participant who grew his own vegetables, and said "That's certainly another advantage of having your own machine, because at this time of year when we are eating lots of lovely fresh stuff, it is good to be able to check it even more regularly, you know." For others, they were grateful to be able to monitor any interactions with other medications they needed to take. Some participants also raised the idea that PSM had given them a greater awareness of their condition, some going as far to say that PSM had made them more conscious of their health in general:

> *For me it was good because, I don't know whether, I had a lot of little operations and things where I would have to give up warfarin for three or four days sort of thing, then you have got to get back on it, and then you have to check the, because you gotta check when you get back on to it… And then I would start a new medication or something, and then that would upset the apple cart so I was continually sort of… the last 12 months I have been all over the ship because I have various little operations and things. Things off here, up here and have to go off warfarin for a few days, you know, and then you gotta get back on it and start all over again. (Marge)*

The ability to check their INR when they desired gave participants the opportunity to decrease the duration of time between tests. The increased testing frequency was in many instances initiated by the participant as they felt that it was important to check their INR control regularly to ensure they remained within their target range.

The increased frequency was perceived by some to enable an increased level of INR control, which translated to increased confidence in their therapy. Olive, an older female participant from Hobart, described her usual care procedure as involving an INR test "about once every six months" when she went to the doctor for new prescriptions. She was someone who appreciated the potential to increase the frequency of testing, "it means I can test it, I test it every month or like less if it is varying a bit I test it more often. You are able to do that and I think it is really good. Because I think when you are on warfarin you really need to know that you are within your range." Joe agreed that self-monitoring increased his frequency of testing, "with this I do it probably twice a week and see the doctor every two or three months, and because not only that but at my age now, I am 66 it sort of, other things you want checked you know, prostate and all that sort of stuff you know". This increased confidence also arose from a decrease in feelings of danger and uncertainty associated with having to wait a specified time before having an INR test performed. Participants also identified a decrease in the anxiety they had previously felt with warfarin therapy as they perceived PSM to have the ability to set their mind at ease. For example, Harold, a pensioner from regional Tasmania, said "it sets your mind at ease, but if anybody, if you hear of anybody and they say [PSM's] not good, they're not right in the head."

The increased confidence in taking warfarin expressed by participants would not have been possible if they were not also confident about the accuracy of the POC device. Participants, like William, expressed a strong confidence in the accuracy of the device, "about two or three times a year he asked me to go to pathology and have it done, it was only about 0.1 or 0.2, say 2.5 and pathology could be 2.6 or 2.4 or something like that, about 0.1 off. Sometimes 0.2 different, apart from that, no hassle what so ever". Joe agreed, saying he would "get it all checked and then find out if it corresponded, like I said, a couple of times it has been dead on. Other times

0.1, what's 0.1? 0.1 is nothing". Some went as far as to say that where their POC results differed from those obtained via usual care, they believed the results they obtained themselves to be the true results. Reasons for this included the process requiring blood samples to be stored and transported and the belief that they are more concerned about themselves and getting an accurate result than a third party would be:

> *I was monitoring myself knowing that my reading was always 0.2 difference from pathology, and I blamed them. I did, I thought it's in the little care and they drive from [here] to [the next suburb] and sometimes to [a suburb much further away] and perhaps, I don't know somewhere else, before they would deliver it back, and I thought, I know they had liquid in the thing to keep the blood in god nick, but I thought aha! Perhaps that's the difference why, it's been hanging around too long. (Ian)*

> *It was always a difference of 0.2 every time, I thought it was because I did mine the night before and then the next day I went to the pathologist, but when I changed that and went to the pathologist straight after I had my own blood test it was still the same, 2 points difference every time I did it, so that was fine. I was sort of a bit more reliant on this than the one from the blood collecting, because I know how that goes having worked in that area. 'Oh there's one in the fridge', so yeah, so I was a bit more, I think it's probably easier to do it straight away. Because they have to collect it and put it in the car and put it in the fridge, so I think it might be a little bit more reliable straight out. (Narelle, former nurse)*

The confidence in the accuracy of the machine translated into a confidence in the ability of some participants to adjust their own treatment. A number of participants were adjusting their own dosages with the support of their GP. The majority of those adjusting their own dose were younger participants who had lifelong

indications for warfarin; however there were some examples of older participants also dosing themselves. For some participants, this confidence did not actually relate to them adjusting their own dose in practice, but having the confidence that they could do it if they needed to. Reasons for not doing their own dose adjustment included a patient held belief that this was the domain of the doctor and not having the support of the GP. However, this did not preclude participants from working out what the doctor was going to say in advance and, in some instances, making suggestions to the GP if the doctor's advice was contrary to their expectations. Participants also felt safe knowing that if their GP was to go away or they were unable to contact them, they would be able to safely dose themselves. PSM was described as the reason they felt able to know what adjustments were needed and was again a great instiller of confidence in the participants:

> *Any changes to the medication were at the doctor's directive, yes. I didn't, although it was fairly obvious that something had gone wonky and it might have been diet, then I'd go to the doctor and follow up on it. And after you've done it for a while of course you get used to the idea, well I think, you know, I should talk to the doctor about whether we reduce the amount of warfarin I take and we did that. (Derek)*

> *Because of monitoring myself, and perhaps because of the years I have been taking this, it also gave me the confidence to say, okay, I know there is about a three day turnaround when you start altering your medications, but I can see that I am down to 1.5 or something dreadful at one point, and I think, well, if I can't get [my GP], I know I have to increase it, but I know I don't take 10mg or something like that. I just creep it up and do it again in three days, or had it been a situation when I hadn't got him, I know I would have perhaps taken 5mg that day and taken [my INR] after 36 hours, say, and just see what had happened*

and then steady out. So I feel fairly confident to do that but goodness me you would never know if you didn't have a machine to do it on. (Wendy)

6.4.2.5.5 Empowerment

Some participants went further than simply expressing an increased in confidence gained through PSM, to expressing a greater sense of self-esteem and empowerment. They described a sense of freedom relating to being able to test their own INR as well as a sense of increased control. Participants also discussed the impact of participating in research and PSM in general.

A feeling of freedom from usual care came through strongly during the interviews. This freedom enabled participants to undertake a range of activities that they would otherwise have not felt able to undertake, or removed a large burden from these activities. Included in the freedom from conventional testing was the ability to adjust their warfarin therapy. While this is discussed above in terms of having the confidence to do the adjustments themselves, this issue also came through as having given some participants a particular sense of empowerment:

I don't really need the doctor at the moment because it's just, I know what to do. Well, I don't need to talk to her, well when I got to see her, she says how's your INR, I say, oh, it is 2.4 or 2.1. She says, oh well, that is good. So, I haven't had to ring anybody up to find out what is going on, because you know, I know better than them, I honestly do, so there was a 2.6, that is about the highest it has been, and that was two in a row and then I didn't change the dosage and it came back to 2.1 next time, so as long as it is within the 2 and 3 I am happy. (Lachlan)

I think I found that it gave me a lot more control over everything, cause my DVT was for no reason, which was a bit nerve racking at the time, but to be able to test [the INR] yourself and then I could adjust my levels as I needed and check in with the GP every now and again… And a lot more control and I guess because

> *we have for the nursing background in our family, we found it quite easy to adjust out doses as we needed, it wasn't a hard thing to do. (Gabby, nursing student whose mother is also a nurse)*

> *We still obviously do it in collaboration but I will manage that on a day to day basis, with my doctor's agreement. These days, I mean in the normal course of things, I will let him know once in a while, once every couple of weeks, how it is going, but I don't ring him up and send him an email saying, hey, I'm only having 5mg today instead of 6, and nor does he want me to, because he is happy that, so it relieves his time as well. (Alex)*

Many participants raised the issue of travelling and the benefits of PSM when planning a trip. Some people described what had happened on previous trips when needing an INR tested while others described having put off trips on account of the need for INR testing. Participants described a freedom associated with being able to travel without needing to be concerned about their INR:

> *…because I have been able to travel with the machine, so [my GP] thinks, you know, lucky you, you can go to, you know, it can give you the freedom to go wherever, so yeah. Last year I went to South America, my husband and I went to South America, we were away for about three months, a few emails plus a short message on the phone a couple of times, when I knew that we would probably be out of internet range, we did a few SMSs… I am thinking, well, you know, if I had to, you know, and I went into, the thought of having blood taken in a South American pathology lab was sort of mind blowing, where has that needle been before and how many times has it been used and so, yeah. (Judith)*

> *We go oversees fairly regularly, probably less so now, I don't know, because Jim is from overseas, and you know, I have spent hours and hours and half a day here and half a day there in clinics in hospitals. Then you get a phone call from them*

> *saying I am sorry it is not good news and all this sort of stuff and you are trying to get into a doctor and it just actually takes over your whole time. This time is was marvellous, I had some terrible results but I felt really quite carefree about it because I know the situation was under control. (Wendy)*

Freedom from usual care was also described in relation to other activities. Some people described the freedom to indulge from time to time in foods or alcohol that they would not otherwise have felt comfortable or safe doing. Others described the advantages of being able to test their INR at home when unwell and not having to travel to a usual care site. Gabby, the youngest of the participants, also raised the freedom it gave her to play sport, without having to arrange INR tests to ensure she was safe to play:

> *I found it gave me, especially I guess as someone a bit younger that likes to go out in the weekends, everybody does, and the alcohol, we go out on a Saturday night and the alcohol just right off, but because I could test it again Sunday, the next day, I could manage it a lot better, it gave me a lot better control over what I was doing. I play a lot of netball too, I have to test it Wednesday afternoon before I play netball on Wednesday night, to make sure that I was in the right range, because I was never allowed to play netball if I was above 3. It gave us a lot more freedom and it meant that we didn't have to go or be down at the GP by 8 o'clock so they could send the test off with the first courier… (Gabby)*

> *I do burst out every now and again with, I love spinach, and I am guilty, I shouldn't tell you this, but I am guilty of sometimes getting a bundle of spinach, [my wife] couldn't eat it, and cooking it in the microwave, draining it off and it has already been cut up. It's a full bunch, putting butter, pepper and salt on it and standing at the sink. [my wife] didn't hear what she doesn't know, and I'll*

> *eat it. I can't help it, and all that vitamin K and thickening things up like glue. If I did feel funny, or feel different, I had that machine to check up. (Ian)*

For some participants, the feelings of empowerment related to a feeling of being in control of their own health. For some, like Mandy, this was important as they have always taken an active interest in their health and feel a need to be in control of whatever aspects they can, "you feel like you have got some say and control of your health, which you need, especially when you're cluey like I am anyway, and not a person who does not know what I am taking". For others, like Tim, it related to an increased confidence associated with having control, "being able to sense that you're not relying on some stranger doing a test… I feel really in control of my own destiny rather than having it placed in someone else's hands". For two male participants, the increased feelings of control lead to significant reductions in feelings of anxiety associated with taking warfarin. These men were overwhelmingly positive about PSM and the considerable positive impact it had had on their lives:

> *I mean to give you, to put the responsibility back in your hands, that is what people want, I think, and when you are not in control, that's what ratchets up the fear and anxiety. I think of all the situations at work where your stress ratchets up, if you are not in control at your work place or whatever, that is what, I think so stress is health y and good, but you know yourself when things, when you are not in control of things or things are out of your control, wow, that is where it becomes destructive… to still have that control and still feel like you are in control is so good. It is another stress that I don't have to worry about in my life. (Terry)*

> *I can only say when I first started on warfarin it was a heck of a weight on my shoulders, it was worrying, and because of that I think when I got this ability to control my own, well at least assess my own, then warfarin didn't worry me*

> *anymore… I really just can't say any more than how the system has changed my life… that was a big load lifted off my shoulders, and I can say that I actually, sounds stupid, but I could feel, once I got the hang of things… I physically felt half an inch taller… Not only did it keep better control of my blood thickness, but it also took better control of the brain, it gave you some sort of relaxant. (Ian)*

Some participants were so satisfied with PSM that they expressed an unprompted desire to recommend PSM to other people taking warfarin. Gordon, a retired GP, mentioned having encouraged other GPs to implement POC testing in their practice. It is said that word of mouth recommendations are the most powerful form of advertising in terms of convincing other people to undertake the same behaviour. The fact that participants were willing to recommend PSM to others supports the notion that they are so satisfied with PSM and its benefits that they were prepared to put their recommendations behind it.

6.5 Discussion

6.5.1 Pharmacist-Based Model Enabling Patient Self-Monitoring of Warfarin

6.5.1.1 Participants

Of the 50 patients who consented to participate in the studies, 48 (96.0%) completed all training requirements and went on to monitor their own warfarin therapy. We defined reasons for dropout during training as either self-exclusion of patients themselves or exclusion by the researcher. Of the 50 consenting patients, one excluded themselves due to a lack of confidence with the responsibility of performing testing. Researchers excluded one patient during training due to a diagnosis of lupus anticoagulant, which is a contraindication to using a POC INR monitor due to potentially inaccurate results with this condition.[402] A further 10 patients consented to participate but were excluded as their GPs refused to consent to their participation. The patients who completed the training had a median age of 65 years – older than those trained in similar PSM studies by Murray *et al.*[260] and Sawicki *et al.*[191]

6.5.1.2 Training for self-monitoring

While PSM is widespread in some countries (it is estimated that 400,000 patients manage their own anticoagulation in Germany),[65] it is virtually non-existent as a management strategy at present in Australia. Hence, there is a need to develop and implement a standardised training program to enable health professionals to train patients who are capable of self-monitoring. It is advantageous to have the opportunity to develop such a training program in Australia before the demand for self-monitoring here becomes established. In Germany, a nationally approved, formalised training program is established. The Association of Self-Management of

Anticoagulation in Germany has established a number of training centres across the country and organises seminars to train the trainers and patients.

Accredited pharmacists in Australia are especially suited to deliver training for PSM in the patient's home. Suitable patients could be identified by the community pharmacist or GP and then be referred to an accredited pharmacist for training. This is the model that was satisfactorily trialled in this study. The training and support piloted in this study were all accepted and there were minimal suggested changes to the materials, indicating that a national program for INR self-monitoring could feasibly be implemented using these materials and support structures.

6.5.1.3 Quality of control of warfarin therapy

There is a strong relationship between TTR and clinical outcomes for patients taking warfarin.[51, 54] A number of peer-reviewed studies have used TTR as a primary outcome measure. The largest of these is the Managing Anticoagulation Services Trial where the decision to use TTR was approved by an external agency for research. [403] Guidelines for defining and measuring high-quality management of anticoagulation therapy recommend using TTR as the primary outcome measure, especially in trial of PSM, with clinical events being regarded as secondary outcomes.[51, 61, 62]

The risk of anticoagulant-induced bleeding is determined by risk factors such as the length of anticoagulant therapy, patient characteristics, the concomitant use of drugs that interfere with haemostasis, and the intensity of anticoagulant effect.[45-47, 105, 136] Control of the INR within the therapeutic range is thus critical to the safety and efficacy of oral anticoagulant use.[2] Better INR control ultimately results in improved clinical outcomes with fewer thromboembolic or bleeding events.[46, 404, 405]

The literature suggests that patients in the community generally spend around 50-60% of their time within the target range.[56] Patients in our study had a baseline TTR of 64.0%. Results from the present study would indicate, albeit in a small number of patients willing to self-monitor, that there is scope for improvement in control. PSM resulted in a significant improvement in TTR in the small study population; the mean TTR rising from 64.0% to 72.9%. This supports the results of a number of studies which have shown PSM to improve the TTR.[130, 149, 190, 237, 245, 248, 249]

The literature also suggests that TTR is closely correlated with outcomes, and improvements in TTR of as little as 10% have been shown to convey a 29% improvement in all-cause mortality.[54, 55, 63, 64, 256] An improvement in TTR of 5-10% has been proposed as a clinically important goal,[51] and was also achieved by the study population.

The greatest benefits from PSM appear to be achieved by those with the poorest initial INR control. In this study population, significantly greater improvements in TTR were obtained by patients who initially exhibited poor control, with TTRs below 60%, with improvements in the range of 30% observed. This finding supports the work of Fitzmaurice *et al*.[256] who found that those patients who exhibited poor control at baseline exhibited significant improvements in control of the magnitude for 15% for those with a target range of 2.0 to 3.0. They concluded that self-monitoring may be the model of choice for those patients who are poorly controlled with routine care.[256] This may be an interesting area for future research which would enable targeting patients at greatest potential of benefiting from PSM.

A number of studies support the notion that increased frequency of INR testing leads to an increased TTR, and improved outcomes.[191, 237, 406, 407] Perhaps the most important evidence illustrating the benefits of more frequent testing arose from Horstkotte[406] where patients went from long to short testing intervals and both

outcomes and patient satisfaction improved. Participants in this study recorded a significant increase in frequency of testing during the intervention period, increasing from a mean of 1.3 to 2.9 INR tests per month. In the absence of any improvements in INR control, the improvement in frequency would have implied improved outcomes for study participants.

6.5.1.4 Accuracy of the CoaguChek®XS compared to the laboratory method

When comparing the accuracy of the CoaguChek®XS to the laboratory method for INR measurement, one problem is the lack of a gold standard for comparison. The laboratory method is fallible and previous studies have found that the variation between portable coagulometers and laboratory was not larger than the variation between different laboratories measuring a single sample.[195] However, for the purposes of this study, comparison to the laboratory was treated as the gold standard.

This method has been used in other studies, examining the accuracy of the CoaguChek®XS compared to laboratory when used by self-monitoring patients. Plesch and van den Besselaar found deviations between the two methods ranging from 6.4%-9.6%,[408] while Torreiro *et al.* found mean differences of 7%.[127] Torreiro *et al.* compared 218 pairs of INR results obtained from 41 patients and found the CoaguChek®XS to be clinically safe and reliable, with a Pearson correlation coefficient of 0.95.[127] Other studies have supported the safety and reliability of the device in the hands of patients, finding Pearson correlation coefficients of 0.91 between the monitor and laboratory test results.[244, 409]

The CoaguChek®XS also performed well in this study. In addition to being highly accurate, participants found it simple to use and both GPs and patients were highly satisfied with its performance. Despite the disadvantage of use by 48 different

users, and comparison with multiple laboratories, the CoaguChek®XS was very accurate compared to the laboratory method, with a Pearson correlation coefficient above 0.94. In this study 98.3% (174 of 177) of CoaguChek®XS INR tests were within 20% and 98.9% (175 of 177) were within 0.5 units of the corresponding laboratory INR, suggesting any variations in the result were unlikely to result in differences in clinical or dosing decisions.

6.5.1.5 Warfarin knowledge

Studies have demonstrated a link between improved warfarin knowledge and outcomes.[137, 141, 405] There was no significant improvement in patient's warfarin knowledge resulting from participation in the PSM study as measured by the OAK Test. However, in the initial study, participants' warfarin knowledge improved significantly from baseline following the education session delivered as part of the training program. This improvement was sustained over the course of the initial six month intervention period with no significant fall in warfarin knowledge between the post education period and the conclusion of the PSM phase.

This supports the notion that a single education session may improve the knowledge of patients regarding their warfarin therapy, but may not be sufficient to result in a sustained improvement. Regular education sessions are likely to be necessary to induce a sustained improvement in knowledge. This is a role that community pharmacists could easily fill when patients present to obtain further supplies of warfarin. Pharmacist-delivered education is likely to be enhanced by the adoption of annual HMRs for patients on warfarin to ensure this knowledge can be consolidated in a familiar environment.

It is also important to note that while the OAK Test is a validated tool for measuring warfarin knowledge,[370] it became evident it may not be an ideal instrument for this task. It became apparent when marking the returned questionnaires that some

patients were penalised for providing an 'incorrect' response that would have been a safe thing to do in practice. For example, question six asks 'When is it safe to take a medication that interacts with warfarin?'. The correct answer is option b, 'If your healthcare provider is aware and checks you INR regularly'. However, many participants responded with option d, 'It is never safe to take a medication that interacts with warfarin'. While this response would be a perfectly safe thing to do in practice, it resulted in them scoring zero for the question as it is not strictly correct. There were two other examples of similar questions. Participants also struggled to answer questions regarding safe levels of alcohol consumption or which over the counter medications were safe to take with warfarin, as many participants did not drink at all or never purchased over the counter medications so had never had cause to learn this information. Given the penalties incurred by patients for responses which would not have been detrimental in practice, it would be beneficial to investigate the use of other instruments, or modification of the OAK Test, for future studies measuring warfarin knowledge.

6.5.1.6 Quality of life

Using the EQ-5D instrument, participants had a median baseline QOL utility of 1.0 (zero tantamount to death, one optimal), which did not change significantly as a results of the intervention. A larger sample size would be required to demonstrate a significant improvement in QOL with PSM using this instrument.

The use of the EQ-5D instrument had advantages in that it was a short, simple tool to administer and one widely used in economic evaluations of health services, however it had disadvantages in being quite non-specific in relation to anticoagulation therapy. An anticoagulation specific QOL instrument, such as the Duke Anticoagulation Satisfaction Scale,[410] might be more suitable for use in future studies.

6.5.1.7 Stakeholder satisfaction

Patients found the PSM model to be a valuable service that made them feel more confident about their warfarin therapy. They found the initial training to be beneficial and agreed that their warfarin knowledge had improved as a result of the training and participation in self-monitoring. Participants also agreed that their overall quality of life had improved as a result of being able to monitor their own warfarin therapy at home and preferred home testing to pathology testing. They found the CoaguChek®XS easy to use and, importantly, agreed that they were confident in the accuracy of the device. These themes came through strongly in the analysis of qualitative data (discussed below).

The GPs who were involved in the study and completed an evaluation questionnaire found it to be a valuable service for their patients. Opinion was divided as to whether they would feel more confident in managing patients on warfarin if this were a regular service; however they agreed more patients could benefit from this type of service. GPs agreed that their patients found the PSM model to be a worthwhile service and also that they coped well with the trial requirements. When asked about their confidence in the accuracy of the CoaguChek®XS, GPs generally agreed that they were confident with its accuracy.

The pharmacists who were involved in the study and completed an evaluation questionnaire were all very positive about the self-monitoring model. They agreed that the PSM model was a valuable service to their patients and felt that the proposed PSM pathway was a feasible way to manage patients on warfarin. Importantly, they all felt confident to identify potentially suitable candidates for PSM and felt that more patients could benefit from this model of care.

6.5.2 Exploration of Patient Views of Self-Monitoring of Warfarin

This is the first known Australian study to explore the perceptions and experiences of patients performing INR self-monitoring from a qualitative perspective. In fact, there was only one paper identified in the published literature that examined patient perspectives of PSM through qualitative methodology.[281] This paper analysed the weblog postings of 108 patients performing self-monitoring, but was hampered by the wide geographical spread of bloggers across different countries and healthcare systems, and an inability to delve further into the reasons behind the posted comments.

This study has found that patients describe the experience of INR self-monitoring in terms of a number of different factors and that the social and demographic factors of individual patients did not appear to impact on the perceptions.

The aim of this study was to explore the experiences and perspectives of individuals undertaking PSM and to answer the question "How are patients experiencing and perceiving self-monitoring?" Five sub-questions were also identified to be addressed. The findings of this study are discussed under the headings of the study questions.

6.5.2.1 How are patients experiencing and perceiving self-monitoring?

The qualitative arm of this study developed from a desire to understand the experiences of the participants in the PSM study. The quantitative feedback suggested that there was a preference among participants for self-monitoring the INR rather than undertaking usual INR monitoring procedures. What could not be explained through these questionnaires was why this preference existed.

Little literature exists to help answer this question. Cromheecke *et al.*[278] stated that PSM was well accepted and appreciated by patients, but did not elaborate as to why.

Anderson *et al.*[192] found that patients in their study expressed a strong preference for PSM due to the increased convenience, reduced pain associated with the testing procedure, and the increased involvement and control over their medical condition. However, these studies both addressed the issue from a quantitative perspective and were unable to delve deeper into additional reasons.

In the first published qualitative analysis of patient perspectives of self-monitoring of the INR, Shah and Robinson identified seven themes emerging from the blog postings of patients, mainly from the USA and the UK, undertaking self-testing.[281] These themes related to patient benefits, equipment related issues, managing the INR, laboratory testing, interaction with healthcare providers, insurance and social issues.[281] Of these a number, such as equipment related issues, laboratory testing and insurance, related to system factors to do with the testing device used and the healthcare environment in which they resided. Others, including patient benefits and interaction with healthcare providers, could be explored to look at how patients are talking about self-monitoring. Patients described a number of benefits including time saved, travel reduction, personal control, choice and freedom, cheaper testing, and peace of mind.[281]

Additionally, a purposive subset of 16 patients from a large study of self-management[256] were interviewed and completed quality of life questionnaires.[411] Eight interviewees had undertaken self-management, while eight were from the control arm of the trial. The interviews covered aspects of daily living, illness, warfarin and self-management (where relevant).[411] Interview data underwent phenomenological analysis. The main theme which emerged was empowerment, linked with changes in feelings of control, knowledge of their disease, and the acquisition of new management skills. All patients received the same education and training, however only those undergoing self-management reported increased

feelings of empowerment, suggesting that it was having the ability to do their own testing was what made the difference.[411]

Overall, patients in the limited published literature and in the current study are talking about PSM in a very favourable manner. Interviewees in this study used positive words and phrases to describe PSM, indicating high levels of satisfaction with the method of management. The benefits described by Shah and Robinson are similar to those raised by interviewees in this study, and could easily be classified within the same themes of convenience, affordability, confidence and empowerment which arose from the interviews. Through exploration of the discussions across those themes, it became clear that self-monitoring had also impacted on aspects of autonomy and independence, quality of life, the experience of living with a chronic illness, self-efficacy, and feelings about taking warfarin.

6.5.2.2 How has self-monitoring changed feelings of autonomy and independence?

The PSM literature reports improvements in patient independence arising from INR self-monitoring.[191, 192, 200, 278, 279] Anderson *et al.*[192] found patients reported an increased sense of involvement and control over their medical condition when performing PSM. These findings were echoed in PSM studies by Kulinna *et al.,*[279] who reported improvements in perceived independence and by Cromheecke *et al.,*[278] who found increased feelings of autonomy resulting from patient independence of anticoagulation clinics.

Participants in this study comprised a mix of people who were happy to play a more passive role and those who preferred to have an active role in their healthcare. Simply by selecting participants of a PSM study, the interviewees were likely to have had an inherent interest in their healthcare compared to others who may have chosen not to commence self-monitoring. Some participants reported PSM gave

them a sense of independence and freedom from the constraints of usual care that enabled them to undertake a range of activities that would otherwise not have been possible. Others reported being grateful for the opportunity to regain some control and say over their health through PSM.

The level of independence experienced by each participant varied, and depended largely on the opinions of the supervising medical professionals and the preferences of the patients themselves. While not all participants wanted to take on an increased level of responsibility and move towards managing their therapy themselves, they all expressed an increased sense of independence to some degree.

PSM emerged as increasing feelings of independence to some degree for all participants by enabling them to move away from a reliance on usual care procedures. Some participants also expressed a sense of regaining autonomy and control over this aspect of their medical care.

6.5.2.3 How has self-monitoring changed perceptions of quality of life?

The term 'quality of life' has come to represent a very structured concept, often utilised in estimating economic differences in different treatment outcomes. It is generally measured by any number of standardised quantitative questionnaires designed for measuring health-related changes in quality of life and is often reported in quantitative literature. Many papers have discussed the impact of self-monitoring of the INR on changes in quality of life.[191, 192, 243, 278-280]

Qualitative research tends to deal with quality of life from a patient perspective, discussing perceived changes in quality of life, or changes in things which may impact on quality of life. In this context, it refers to:

> *An individual's sense of social, emotional and physical well-being which influences the extent to which she or he can achieve personal satisfaction with their life circumstances.*[412]

One study looking at perspectives of patients taking warfarin explored the psychological impact of taking warfarin.[273] They described the psychological impact of taking warfarin varying between patients, but that the potential for bleeding and food and medication interactions with warfarin having a great psychological impact.[273] The result of this psychological impact could be argued to be a reduced quality of life.

To date only one published study has touched on the impact of PSM on quality of life from a qualitative perspective. This paper by Shah and Robinson[281] included a small discussion of the social and psychological issues for patients performing INR self-monitoring. Due to the nature of the study, a content analysis of weblogs, this issue could not be explored in depth, and little about the effect of PSM on quality of life was included.[281]

The current study did not directly target quality of life through specific measures during the interviews, but found that participants did discuss PSM in terms that suggested that it had improved their overall quality of life. Improvements were seen in participants' confidence to travel and in taking warfarin, in their measures of convenience and their feelings of empowerment, all potential surrogate markers for quality of life. Quality of life was also reported by participants to have improved during the quantitative evaluation questionnaires; however, this did not come through when using the formal, though arguably insensitive, EQ-5D quality of life instrument. The discussions arising during the interviews support the self-reported improvements in quality of life and suggest that these improvements could have arisen through a range of perceived benefits associated with PSM.

6.5.2.4 How has self-monitoring changed the experience of living with a chronic illness?

The experience of living with a chronic illness is complex and shaped by the individual's social and cultural factors, in addition to the specific aspects of the illness itself.[412] For many it involves developing both means by which to cope with the illness and its medical management, and strategies by which to manage the illness as a part of their life.[413]

Many participants in this study had concomitant illnesses to cope with in addition to their indication for warfarin. They generally expressed that having an additional illness impacted negatively on their experience of taking warfarin or contributed to an increased anxiety associated with warfarin therapy. Anxiety at the potential effects of warfarin was also expressed in a Canadian qualitative study of patient perspectives of taking warfarin.[272]

Furthermore, participants generally reported the monitoring requirements associated with the usual care of management of warfarin to be inconvenient, and at times associated with negative effects such as bruising and scarring. This made the experience of managing their chronic medication, and hence managing their chronic illness, a greater burden. Participants in another study of patient perspectives of taking warfarin also expressed the monitoring procedures associated with warfarin as burdensome.[273]

PSM emerged as improving the experience of living with a chronic illness. Participants reported that PSM acted to alleviate the stress of taking warfarin and, for two participants in particular, significantly reduced the anxiety they felt at having to take warfarin on top of managing their other conditions. The burden associated with usual care monitoring was also reported to be alleviated, or at the least vastly improved, through the availability of PSM. These improvements in the

experience of living with a chronic illness through self-monitoring were also observed by Shah and Robinson in their qualitative analysis of blogs.[281] Bloggers reported reductions in the logistical burdens of INR testing and an improved sense of peace of mind.[281]

PSM can be seen to have greatly improved the experience of living with a chronic illness for people taking warfarin.

6.5.2.5 How has self-monitoring changed feelings of self-efficacy?

Perceived self-efficacy has been defined as:

> *People's beliefs about their capabilities to produce designated levels of performance that exercise influence over events that affect their lives. Self-efficacy beliefs determine how people feel, think, motivate themselves and behave.*[414]

Very little has been reported in the literature about the effects of taking warfarin on people's perceptions of self-efficacy. Two studies were identified, Sawicki[191] and Cromheecke *et al.*[278], which both reported PSM of warfarin therapy resulted in increased measures of self-efficacy, as determined by a quantitative questionnaire.

While self-efficacy was not targeted by specific questions during the course of the qualitative interviews in this study, the responses of the participants suggest that perceptions of self-efficacy did improve. This improvement is demonstrated by the increases in confidence and feelings of empowerment that were evident in patient's narratives.

The ability to measure their INR emerged as providing them with the capability to influence a level of control over their lives, be it through simply measuring and knowing their INR, or through having the ability to adjust their own dose. PSM also came through as enabling participants to have control over where and when they

test their INR, how and where they can travel, and what foods and other medications they can safely take while on warfarin. Self-monitoring appears to increase patient perceptions of self-efficacy through enabling them to have the ability to take back some control over aspects of their health.

6.5.2.6 How has self-monitoring changed feelings about taking warfarin?

Feelings about taking warfarin expressed by participants mainly related to the time before they commenced PSM and were generally quite negative and laced with fear. The fears often related to fears of the side-effects associated with warfarin. It was identified that much of the education received by participants when commencing warfarin was suboptimal, and at times caused more concern than comfort. Bajorek *et al.*[271] identified similar educational concerns in a qualitative study of older patients. Patients in their study requested more information about warfarin therapy, as they felt access to information to be inadequate, particularly from their GP and pharmacist.[271] They felt that improved education would increase their confidence in taking warfarin.

PSM, and the associated education and training program used in this study, improved patients feelings about taking warfarin. It reduced the perceived inconvenience associated with having to attend INR tests and removed the negative effects that were described as being experienced with venous sampling. Self-monitoring also improved patients' overall confidence, particularly their confidence with taking warfarin. Improvements in confidence resulted from the ability to closely monitor their INR and, in some cases, adjust their warfarin dose. Sidhu and O'Kane's finding supported these views, with patients in their study reporting greater personal convenience, more confidence in their therapy and the ability to travel with less fear of INR fluctuations.[245]

Overall, PSM appears to have impacted positively on patients' feelings about taking warfarin.

6.6 Facilitating Patient Self-Monitoring of Warfarin

The primary aim of this study was to develop, implement and evaluate a pharmacist-inclusive pathway to enable Australians who take warfarin to monitor their own therapy. To this end a wide range of training and educational resources were developed and used to pilot the model. The materials were well received by all participants and received positive reviews from stakeholder organisations. Feedback on the proposed model from participants and stakeholders was also positive. The proposed pathway was demonstrated to enable the successful selection of suitable candidates for PSM, to deliver appropriate, patient-centred education and training, and to ensure quality control procedures are in place. The model was also shown to clinically improve measures of INR control, including TTR.

It also aimed to compare and contrast the results of both the quantitative and qualitative data collection methods used to explore the outcomes and experiences of PSM. The adoption of a mixed methods design was utilised to test the theory that PSM can improve outcomes for people taking warfarin in Australia and to describe the benefits of INR self-monitoring from both objective and subjective perspectives.

The main benefit of PSM found in this study was apparent through both methods of data collection. While the study was not powered to detect differences in the rates of clinical outcomes, such as major bleeding events and thromboembolic complications between the pre-study and intervention periods, it was powered to detect differences in measures of INR control. Measures of INR control improved during the PSM intervention period, with an increase in the frequency of INR testing, to around double the frequency seen in the control period, and an average improvement in the TTR of 9%.

It has been suggested that measures of INR control, in particular TTR, should be used as the primary outcome measure in trials of PSM, with changes in event rates

being reported as secondary outcomes.[51] This recommendation is accompanied by the suggestion that improvements in TTR of 5-10% are clinically significant goals,[51] as the time spent within the therapeutic ranges is widely accepted as being predictive of adverse events.[61] Event rates have been modelled against INR control and increase approximately exponentially as the INR moves further from the target range.[51]

The quantitative component of this study demonstrated an increase in TTR for participating patients, which is likely to translate to improvements in clinical outcomes, hence reducing the burden of living with a chronic illness. The qualitative data supported these findings, with participating patients describing the impact PSM had had on their experiences of living with a chronic illness.

PSM emerged in the qualitative data as improving the experience of living with a chronic illness by acting to alleviate the stress of taking warfarin and reduce the anxiety of having to take warfarin on top of managing other conditions. The burden associated with usual care INR monitoring was also reported to be alleviated, or at the least vastly improved, through the availability of PSM.

The quantitative study was not powered to objectively show any changes in quality of life arising from PSM, despite this measurement being conducted as part of the data collection. This lack of power related in part to the sensitivity of the formal quality of life instrument used and in part to the small number of participants who took part in the study. Despite the EQ-5D tool not uncovering any changes in quality of life occurring during the PSM intervention, participants did report subjective improvements in quality of life associated with PSM.

While the interviews did not directly target quality of life through specific measures, it was found that participants did discuss PSM in terms that suggested that it had improved their overall quality of life. Improvements were seen in participants'

confidence taking warfarin, in convenience and in feelings of empowerment, all potential surrogate markers for quality of life. The discussions arising during the interviews support the notion that PSM resulted in improvements in quality of life and suggest that these improvements may have arisen as a result of the perceived benefits associated with PSM.

The other benefits of PSM that arose during this study are ones which are unable to be extensively explored, or even detected, through the use of quantitative data collection methods. Purely subjective benefits of PSM that emerged during the qualitative investigation were increased feelings of autonomy and independence, improvements in feelings of self-efficacy and taking warfarin, arising through improvements in patient confidence, convenience and empowerment. Despite being very subjective in nature, these benefits support the theory that PSM improves outcomes, particularly patient-centred outcomes, for people taking warfarin in Australia.

High levels of satisfaction with the PSM model emerged both from the quantitative evaluations of stakeholders and the qualitative interviews with the patients. This satisfaction indicates a high level of support for the introduction of a similar model of PSM used in the study to facilitate the wider uptake of PSM in Australia.

Qualitative and quantitative feedback both suggest that the proposed clinical pathway for PSM is likely to a feasible model to implement within the Australian healthcare setting.

This model could be implemented in Australia under existing funding structures, with community pharmacists in an ideal position to screen and refer patients to their GP to discuss the concept of PSM. This discussion would occur with the view to referring the patient to a trained accredited pharmacist for specialised training, delivered as part of an HMR.

6.6.1 Limitations of the study

The quantitative phase of this study was designed as a historically controlled proof of concept trial to determine the feasibility of implementing a model of care involving pharmacist-delivery of warfarin self-monitoring training. While the study involved only 48 patients, it was sufficiently powered to detect an improvement in TTR. Potential limitations of the study include the method of selection of patients, the small sample size, non-randomised design, and the relatively short duration of the intervention. Patients were selected in a similar way to other trials involving PSM of warfarin therapy, [256, 260] but involved community pharmacists identifying participants and inviting them to participate instead of primary care physicians. GPs indicated that in any program involving PSM they would need to be the gatekeepers and the ones who are responsible for deciding which patients can participate in PSM.

As with other trials of PSM,[256, 260] participants in this study were hand selected by their health professional. They were a highly motivated group of patients who had an interest in becoming more involved in their healthcare, and as such cannot be expected to be representative of the general population of people taking warfarin. This is not strictly a limitation as it has never been suggested that PSM is a model of management suitable for all patients, but rather it is a management strategy that improves patient adherence, satisfaction, and clinical outcomes in those patients who wish to undertake self-monitoring.[143]

Participants in the study obtained much of their support from the research team during phone calls to follow up on INR results. In a program to implement PSM more broadly patients would need to obtain this support from their community pharmacist or GP, and health professionals may need to be educated to provide this support.

Additionally, it must be remembered that the majority of the participants in this study performed self-monitoring rather than self-management, meaning most were still reliant on their healthcare professional for dose adjustments and decision making. This is likely to have impacted on their perceptions of self-monitoring, their knowledge, satisfaction, and feelings of self-efficacy.

Despite the strengths of the qualitative aspect of this study, it is important to acknowledge the existence of a number of limitations. Although participants in qualitative studies are not intended to be a representative sample, our sample consisted of a highly selected patient population who either self-selected for participation in the PSM study or were selected by their health professionals on the basis of being actively interested in their healthcare. As such, they represented a group of patients who were likely to have had an existing interest in their own health. These were patients who had persisted with self-monitoring for up to two years, suggesting they were positive about the process. Patients who were not so positive about the experience of self-monitoring would likely have not persisted with PSM for so long and would have been likely to have held different opinions. It is interesting to note, however, that no patients self-withdrew from the PSM study.

Additionally, while rapport built by the researcher with the participants was undoubtedly a strength of this study, enabling participants to respond openly and honestly about the way they felt about the experiences of self-monitoring, it could also be considered as a possible weakness. The participants had, in many instances, had many opportunities to interact with the researcher and develop an understanding of the researcher's opinions on PSM. This may have influenced how the participants responded and potentially influenced participants to alter their narrative to reflect what they thought the researcher expected to hear.

6.6.2 Conclusion

The use of a triangulation mixed methods design enabled complementary quantitative and qualitative data to be collected on the same topic. This drew on the strengths of both forms of research to describe the benefit of PSM from both objective and subjective perspectives.

This study successfully demonstrated the feasibility of the proposed clinical pathway to enable PSM of warfarin therapy. Measures of INR control, including TTR, and subjective patient outcomes were improved during the PSM phase. The level of satisfaction expressed by all groups of participants in regard to both the study materials and the method of management was very high, supporting the implementation of a national program to enable INR self-monitoring in Australia.

This study aimed to increase the understanding of patient experiences of self-monitoring through exploring how patients are talking about PSM and whether PSM has impacted on various aspects of their lives. It was found that patients talk about PSM in a very positive light. They described it passionately, as something of value, which reduced their anxiety about taking warfarin and freed them to get on with their lives.

Self-monitoring was found to reduce inconvenience associated with usual care models of warfarin management. It reduced the need to travel to testing sites, the adverse effects associated with venous sampling procedures and reduced the impact of INR testing on other activities such as travel and work commitments. It was also described as much easier than conventional management.

In addition to improving convenience for patients, self-monitoring was found to increase confidence with warfarin treatment. Confidence arose from the ability to check if the INR is out of the target range, through decreasing feelings of uncertainty

and anxiety and through a satisfaction with the accuracy of the POC device and the assurance this provided. For some, PSM was also found to increase their self-esteem and feelings of empowerment through freeing them from a reliance on usual care procedures and an increased sense of control.

Looking more closely at the data it became clear that self-monitoring had also had positive effects on other areas of patients' lives. It improved feelings of autonomy and independence through enabling an increased perception of being in control. PSM improved patient perceptions of quality of life and improved the experience of living with a chronic illness for patients by alleviating some of the stress and inconvenience associated with warfarin management. Perceptions of self-efficacy also improved as patients took back control over one aspect of their medical care. PSM also improved patients' feelings about taking warfarin through improving their confidence and reducing the inconvenience of usual care.

Overall, this study provided an insight into the lived experience of self-monitoring of warfarin therapy as gleaned from the unique perspective of a group of patients performing this method of management. It found PSM, in addition to improving control of warfarin therapy, had a positive effect on the experiences of the participants. This is a significant contribution to the body of knowledge as no other similar study could be found in the published literature.

It is apparent from this study that PSM improves both the clinical and patient-centred outcomes of warfarin.

PART FOUR: THE FUTURE OF ANTICOAGULATION MANAGEMENT IN AUSTRALIA

Chapter 7 : An exploration of optimising warfarin management

7.1 Pharmacist-delivered services to optimise warfarin management

Warfarin therapy may be managed by a variety of professionals in a variety of settings, including office-based management by primary care physicians, management by pathology laboratories, through specialist anticoagulation clinics, and by the patient themselves in partnership with their healthcare providers.[12] Management in Australia has tended to focus on the traditional office and pathology-based models. However, internationally alternative models of care are playing an increasingly significant role with very positive results.

The focus of the profession of pharmacy has been evolving over the past century, as the role of pharmacists transitions from one of a compounder, through one of a supplier, to one of a deliverer of professional services. Much of the focus of the pharmacy profession moving forward will build on the concepts of pharmaceutical care and quality use of medicines. Internationally, this shift has begun, with pharmacists having been shown to be effective in improving the quality use of warfarin through a variety of professional service delivery models.[329] Yet in Australia, pharmacists currently play little or no role in warfarin management.

The main objective of this thesis was to examine the effect of using pharmacist-delivered models of care on warfarin management within Australia. To achieve this objective, a number of complementary projects were required to determine the current state of warfarin management in Australia, and to explore areas of warfarin management that pharmacists could help to improve. The projects focussed on the

role of pharmacists in improving patient education, increasing access to INR testing and facilitating PSM.

The quality of warfarin management is measured through a calculation of the proportion of time a patient's INR spends within the target INR range for their condition. Ideally the therapeutic goal of management should be for 100% of INRs to be in range, although it has been stated that a realistic and achievable aim is a TTR of upwards of 60% to 70%.[61, 62] Internationally, community-based studies consistently demonstrate suboptimal levels of INR control of around 50-60%,[56] although little data is available on the level of control achieved through usual models of care in Australia. To date, the largest published data on INR control in an Australian setting comes from the PoCT where 944 patients received either usual care management through pathology testing, or POC INR testing in their GPs office.[68] Regardless of the model of care, the average TTR across both groups for the intervention period was 68%. However, data which has recently emerged from the Australian sites of the Randomised Evaluation of Long-Term Anticoagulation Therapy (RE-LY) study investigating the use of the new oral anticoagulant agent, dabigatran, suggests INR control of community-based patients on warfarin may be closer to 74%.[415]

To explore the INR control of a community-managed population unaffected by study setting, a retrospective cross-sectional study of INR results of 442 Australian veterans over a three year period was undertaken. The mean TTR was 61.8% in this population; control comparable to the TTRs achieved in RCTs,[56] which generally involve a younger, healthier cohort. This suggested there may be a potential role for strategies aiming to improve INR control among Australian patients in line with best practice guidelines.

Review of the literature suggested pharmacists could play a role in improving warfarin management through optimising the delivery of education, improving access to INR testing and facilitating PSM.[12, 205-209]

Studies have demonstrated strong links between receiving quality warfarin education and levels of warfarin knowledge,[133-136] and the level of warfarin knowledge and INR control and clinical outcomes.[84, 136, 137, 141] Computer-based education has been identified as an effective strategy for increasing health knowledge and the adoption of healthy behaviours, with around 50% of people now using the internet to obtain medical information.[163-165]

A website was designed to provide patients and health professionals with educational resources regarding anticoagulation and to promote PSM as a management option. The site aimed to be a comprehensive and reliable online resource and was promoted directly to pharmacists across Australia. It received high levels of utilisation and positive feedback from health professionals and patients, and proved to be an important educational resource that was an easy and accessible tool for pharmacists to use to complement face to face counselling services and further improve patients' knowledge about warfarin therapy and PSM.

Community pharmacists are in a unique position to help patients manage chronic therapies such as warfarin, in view of their expertise, their regular contact with patients and their accessibility. Internationally, pharmacists run anticoagulation clinics in community pharmacies with impressive outcomes, especially in regards to INR control.[329, 331] Most recently, a pilot study was conducted in a small rural town in New Zealand to assess the feasibility and potential benefits of managing warfarin through a pharmacist using POC testing and online computer decision support.[337] The outcomes of this pilot resulted in the service being expanded and funded through the New Zealand government to further assess the feasibility of introducing

pharmacist-run anticoagulation clinics into community pharmacies across the country.

Tools and resources were developed to improve access to INR testing by facilitating the introduction of enhanced anticoagulation services, including pharmacy-based INR clinics, in Australia. The resources covered POC INR theory, liaison strategies, business models, standard operating procedures and a Toolkit of templates, and were supported by the website described above. A pilot was conducted in three rural community pharmacies, with a subsequent project involving 36 pharmacies. While the resources received positive feedback from participating pharmacists, the rate of successful service implementation was low. Factors impacting on service implementation included pressures on pharmacist time and a lack of liaison with local healthcare providers. Additionally, despite the perceived benefits of such services to the participating communities, the current model of healthcare remuneration in Australia impacted on the long-term financial viability of such services.

PSM of warfarin therapy reduces the harms and maximises the benefits of anticoagulation.[234] PSM has been shown to improve INR control, clinical outcomes, and patient-centred outcomes such as knowledge and quality of life.[234] It is a model of care which is subsidised to varying extents in many healthcare systems internationally, yet receives no subsidisation under the Australian healthcare model.

The adoption of PSM to achieve appropriate outpatient anticoagulation and prevent complications was ranked in the top 10 clear opportunities to improve patient safety in a report prepared by the US Agency for Healthcare Research and Quality over 10 years ago.[241] The underuse of PSM is now evidence of a practice gap in Australian healthcare and represents a clear opportunity for pharmacists to facilitate the uptake of this model of care.

Development, implementation and evaluation of a pharmacist-centred pathway to enable PSM were undertaken. Forty-eight patients successfully underwent training and participated in PSM for a median of 16.9 months. INR control data during PSM was compared to that from the six months prior to entering the study for 46 of the 48 patients. There was a significant improvement in INR control, with the mean TTR increasing from 64.0% to 72.9%. The level of satisfaction expressed by all patients and healthcare professionals in regards to the training materials, the method of management and the pharmacist-delivered model was high, supporting their use as part of a national program to enable PSM in Australia.

Most studies examining patient perspectives of PSM have used surveys or other quantitative methods. However, given the inherent complexity of the lived experiences of patients, qualitative research methods are likely to provide additional insight. A comprehensive literature search identified only one qualitative investigation of patient perspectives and experiences of PSM explored through an analysis of internet blog postings.[281]

Clinical data analysis of PSM was complemented by a qualitative exploration of 38 patients' experiences of self-monitoring and the impact of PSM on various aspects of their lives. It was found that patients discussed PSM positively.

Self-monitoring reduced the anxiety associated with taking warfarin, reduced the inconvenience associated with the patients' usual care model of management, and increased confidence with warfarin treatment. It improved feelings of autonomy and independence through enabling the perception of increased control. PSM improved patient perceptions of quality of life and improved the experience of living with a chronic illness for patients by alleviating some of the stress and inconvenience associated with managing warfarin therapy. Perceptions of self-efficacy also improved as patients took back control of one aspect of their medical

care. Despite the wide range of patient-centred benefits reported as a result of PSM, not all patients felt they would be able to afford to continue undertaking PSM outside of the trial, and many could not understand the lack of remuneration for PSM available through the healthcare system.

It must be remembered that the majority of the participants in this study performed self-monitoring rather than self-management, meaning most were still reliant on their healthcare professional for dose adjustments and decision making. This is likely to have impacted on their perceptions of self-monitoring, their knowledge, satisfaction, and feelings of self-efficacy. If self-management were pursued as a management option for a greater number of patients, it is likely that patients would express an even greater degree of positivity towards the alternative method of warfarin monitoring.

The positive results arising from these projects suggest there is likely to be a role for pharmacist-delivered services in improving the management of warfarin in Australia.

7.2 Emerging options in anticoagulation

Vitamin K antagonists, such as warfarin, have been in use for more than 50 years and, up until recently, were the only oral anticoagulants available.[14] As discussed in earlier chapters, the use of vitamin K antagonists is limited by the difficulties managing them, the requirement for frequent monitoring of the INR, the necessity for dose adjustments in response to INR variations, the variable pharmacology and plethora of food and drug interactions.[14] These difficulties have contributed to an underuse of warfarin, particularly in the elderly,[222] and to the search for new oral anticoagulant agents.[416]

Warfarin exerts its actions through inhibiting the production of vitamin-K dependent clotting factors, namely factors II, VII, IX, and X, thus acting on multiple targets within the clotting cascade.[4][17] It is thought that its actions on multiple factors, and that each factor has a different half-life, could explain, in part, the unpredictable anticoagulation effects sometimes seen with warfarin.[14] Hence, efforts in the search for new oral anticoagulants which exhibit more predictable actions than warfarin have focussed on the direct inhibition of single clotting factors, namely factor II (thrombin) and factor Xa.[14]

It is likely that the new generation of oral anticoagulants will have many advantages over traditional anticoagulants like warfarin. Because the new agents are targeting one specific factor in the clotting cascade, their pharmacology is likely to be more predictable, reducing or negating the need for monitoring.[14] This will translate to a single dose regimen that will not need to change in response to monitoring and to fewer food and drug interactions. Also, because they act directly on coagulation factors, inhibiting those factors already present in the circulation, they will have a shorter onset of action than warfarin, which inhibits clotting factor production and must wait for existing factors to be removed from the circulation before its effects are evident.

The first oral direct thrombin inhibitor to be released was ximelagatran, which was launched in Europe in 2004.[14] It's lifespan was short however, being withdrawn from the European market in 2006 in response to potentially fatal hepatotoxicity and rebound cardiovascular events, and never achieving regulatory approval in the USA or Australia.[14] Since the removal of ximelagatran from the market, a number of new oral anticoagulant agents, targeting either thrombin or factor Xa, have started to make their way into the arena. The three agents leading the way are rivaroxaban

and apixaban, direct factor Xa inhibitors, and dabigatran, a direct thrombin inhibitor (Table 34).

Table 34: Characteristics of new oral anticoagulants compared with warfarin (Adapted from Altman and Vidal[418] and Potpara and Lip[419])

	Warfarin	Dabigatran	Apixaban	Rivaroxaban
Main action	Inhibition of synthesis of vitamin K-dependent factors	Anti-factor IIa	Anti-factor Xa	Anti-factor Xa
Bioavailability (%)	>95	~6	>50	>80
Half-life (h)	35-45	12-17	8-15	5-9
Renal clearance (%)	0	80	25	66
Protein binding (%)	99	35	87	>90
Interactions	CYP2C9, 3A4, 1A2 inhibitors, dietary vitamin K	P-gp inhibitors*, PPIs**	Potent CYP3A4 inhibitors***	Potent CYP3A4 inhibitors, P-gp inhibitors
Dosing in AF	Adjusted to INR, once daily	Twice daily	Twice daily	Once daily

**P-gp = P-glycoprotein; inhibitors include quinidine, verapamil, ketoconazole, macrolides*
***PPIs = Proton pump inhibitors*
****include ritonavir and ketoconazole*

At the time of writing, both dabigatran and rivaroxaban have been approved for use in Australia by the Therapeutic Goods Administration (TGA) and listed on the PBS for the prevention of VTE following major orthopaedic surgery. Dabigatran has also been approved by the TGA for use for stroke prevention in patients with AF, but is awaiting PBS listing for this indication. Results have recently been published the for use of both apixaban[420] and for rivaroxaban[421] for stroke prevention in AF compared to warfarin (Table 35). This will no doubt see these agents applying for approval for use in stroke prevention in AF in Australia in the months to come.

The approval of dabigatran in Australia for stroke prevention in patients with AF is supported by the results of the RE-LY study.[422] This unblinded clinical trial randomly assigned patients to dabigatran or warfarin and compared the clinical

outcomes. Patients in the dabigatran arm received either 110mg or 150mg twice daily, while warfarin was dosed according to the INR.

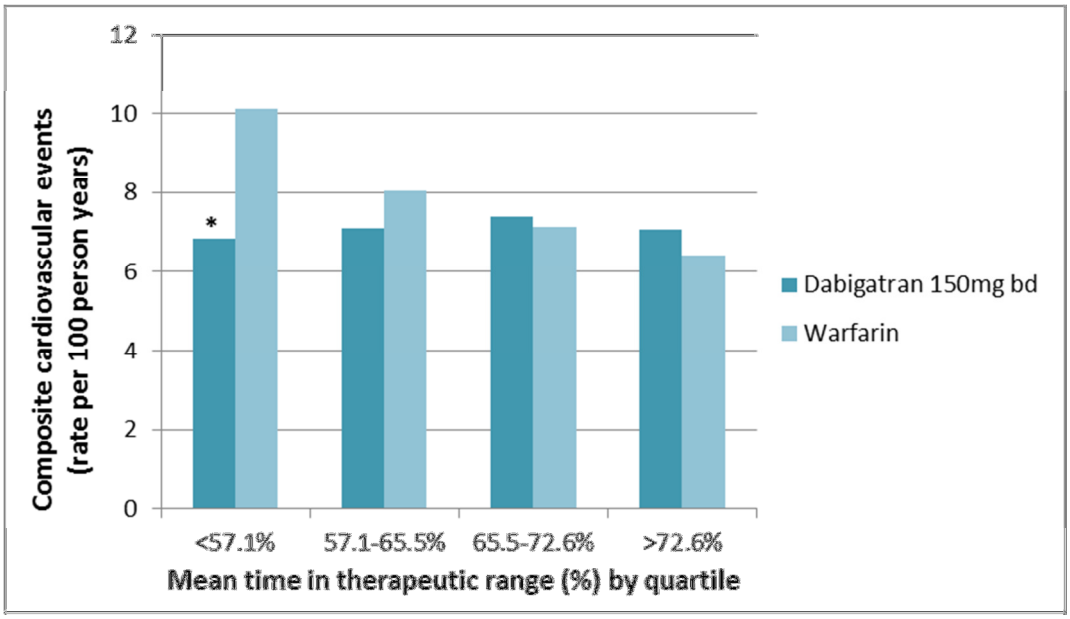
They found that patients assigned to 150mg twice daily of dabigatran had a significantly lower rate of ischaemic stroke, and no additional risk of major bleeding compared to those taking warfarin (0.6%pa absolute risk reduction).[422] Dabigatran also caused significantly fewer intracerebral haemorrhages, yet increased the rate of symptomatic dyspepsia and myocardial infarction.[422] Those patients taking 110mg twice daily of dabigatran experienced lower rates of major bleeding to those taking warfarin with similar rates of stroke and systemic embolism.[422] These results suggest that different doses of dabigatran may be appropriate for use in patients depending on an assessment of their individual risk of bleeding compared to their risk of embolism.

The US Food and Drug Administration was satisfied of a positive benefit to harm balance for dabigatran but failed to identify a subgroup of patients in which the benefit-harm profile was superior for the lower dose and consequently only approved the 150mg twice daily dose.[423] However, both doses have been approved by other regulatory authorities.[424, 425] The European Medicines Agency specifies 150mg twice daily for those under 80 years of age and 110mg for those over 80 years of age or as an option when the thromboembolic risk is considered to be low and the risk of bleeding is high.[424]

An important factor to note is the average TTR achieved by patients in the warfarin arm of the RE-LY trial was 64%.[422] While this is comparable to many community-based studies as has been previously discussed, this supports the notion that there is considerable room for improvement in the overall management of warfarin therapy which would impact on the relative superiority of dabigatran as a comparator agent.

Post-hoc analysis of the RE-LY trial examined the difference in composite cardiovascular events, including stroke, systemic embolism, pulmonary embolism, myocardial infarction, death and major bleeding, at different levels of INR control. These analyses showed that dabigatran 150mg twice daily significantly reduced the rate of composite cardiovascular events at study sites where the INR control was poor but not at sites where INR control was better (Figure 37).[415] The average INR control achieved by patients being managed at Australian sites of the RE-LY study was 74%,[415] suggesting that Australian patients may be less likely to experience a clinical benefit from changing anticoagulant agents from warfarin to dabigatran.

Figure 37: Rate of composite cardiovascular events¥ relative to mean time in therapeutic range.[415]



* $p<0.05$ versus warfarin

The results of the Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared with Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation (ROCKET AF) study were recently published after a lengthy delay.[421] This double blinded clinical trial randomly assigned patients to rivaroxaban 20mg daily or warfarin (dosed according to the INR) and compared the clinical outcomes.

Rivaroxaban was shown to be non-inferior to warfarin in preventing stroke, but the superiority analysis drew questions when, in the intention-to-treat group, the drug failed to demonstrate statistical superiority over warfarin, although rivaroxaban was statistically superior in an "as-treated" analysis.[421] Intracranial and fatal bleeding was shown to be lower with rivaroxaban, while other major bleeding was similar to warfarin.[421] The performance of multiple analyses has complicated the interpretation of the findings of the ROCKET AF study.

It is possible that the failure of ROCKET AF to demonstrate superiority of rivaroxaban over warfarin is due in part to the once daily dosing regimen chosen for the trial. Of all the new oral anticoagulant agents, rivaroxaban has the shortest half-life yet was dosed only once a day. This single daily dosing would have potentially resulted in periods of the day where a state of less than optimal anticoagulation existed. Additionally, missing one dose of rivaroxaban would result in a much bigger impact on anticoagulation status than missing a dose of an agent being dosed twice daily or warfarin with its long half-life and duration of action.

It is also possible that the non-superiority of rivaroxaban can be explained in part by the patients enrolled in ROCKET AF being at a higher risk of stroke or systemic embolism than those enrolled in the comparator trials, with a mean $CHADS_2$ score of 3.5.[421] Yet, ROCKET AF also had the poorest INR control in the warfarin arm of any of the trials, with a mean TTR of 57.8%, which should have given rivaroxaban some degree of advantage over the other agents.[421] Without head to head comparison studies between the agents it is difficult to determine which of these agents is likely to be the safest and most efficacious replacement for warfarin.

Most recently, the results for the Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation (ARISTOTLE) trial have been published.[420] This double blinded clinical trial randomly assigned patients to

apixaban 5mg twice daily or warfarin (again dosed according to INR) and compared the clinical outcomes.

It was found that apixaban was associated with a 21% reduction in the risk of stroke or systemic embolism, a 31% reduction in bleeding, and an 11% reduction in all-cause mortality.[420] While both dabigatran and rivaroxaban have shown some benefit over warfarin in the RE-LY and ROCKET AF trials, apixaban is the first of the new agents to have shown definite reductions in each of the major outcomes of stroke, bleeding, and mortality.[420]

An important factor to note is the average TTR achieved by patients in the warfarin arm of the ARISTOTLE trial was similar to that achieved in RE-LY, with a mean of 62%.[420] This continues to support the notion that there is considerable room for improvement in the overall management of warfarin therapy which would impact on the relative superiority of any of the new anticoagulants as comparator agents. Post-hoc analyses of the ARISTOTLE trial are yet to be published; however, the differences in composite cardiovascular events, including stroke, systemic embolism, pulmonary embolism, myocardial infarction, death and major bleeding, at different levels of INR control is currently being explored. Data presented at the European Society of Cardiology Congress earlier this year suggests that the benefits of apixaban over warfarin in preventing stroke, reducing bleeding and improving survival appear consistent regardless of the centres' quality of INR control.[426] The data also showed that the TTR achieved by Australian sites in the trial was not significantly different to the overall mean TTR of 62% used in the analysis, suggesting that Australian patients are likely to experience similar clinical benefits of apixaban as the overall ARISTOTLE results imply.[426]

Table 35: Completed, randomised trials with new oral anticoagulants in AF compared to warfarin (INR 2.0-3.0)[420-422]

	Trial (N)		
	RE-LY (18,113)	**ROCKET AF (14,264)**	**ARISTOTLE (18,201)**
Drug and doses	Dabigatran 110mg/150mg bd	Rivaroxaban 20mg daily	Apixaban 5mg bd
Design	Open-labelled, non-inferiority	Double-blind, non-inferiority	Double-blind, non-inferiority
Mean age (years)	71.5	73	70 (median)
TTR with warfarin (%)	64	57.8	62.2
Warfarin-naïve (%)	50.4	37.5	43
Mean $CHADS_2$	2.1	3.5	2.1
Previous strokes or TIAs (%)	20	55	19
Primary end point (stroke or systemic embolism)	1.71% warfarin 1.54% D-110mg (*p*=0.34) 1.11% D-150mg **(*p*<0.001)**	2.42% warfarin 2.12% rivaroxaban (*p*=0.117)	1.60% warfarin 1.27% apixaban **(*p*<0.001)**
Major bleeding events	3.57% warfarin 2.87% D-110mg **(*p*=0.003)** 1.11% D-150mg (*p*=0.31)	3.45% warfarin 3.6% rivaroxaban (*p*=0.576)	3.09% warfarin 2.31% apixaban **(*p*<0.001)**
Intracranial haemorrhage (% per year)	0.74% warfarin 0.23% D-110mg **(*p*<0.001)** 0.30% D-150mg **(*p*<0.001)**	0.74% warfarin 0.49% rivaroxaban **(*p*=0.019)**	0.80% warfarin 0.33% apixaban **(*p*<0.001)**

Yet despite the expected and apparent benefits with the new oral anticoagulants, there are also several factors which may make their use in clinical practice more troublesome than first expected. These factors include:

- The newer agents have a shorter half-life and duration of action;[427] dabigatran and apixaban are administered twice daily. Non-compliance with anticoagulation is a widely recognised problem in clinical practice,[428] this is likely to be amplified for medications that must be taken twice a day,

resulting in higher probabilities of missed doses and suboptimal anticoagulation.[427]

- While the need for regular testing of the INR has been cited as an inconvenience of warfarin therapy, it has enabled the identification of states of over and under anticoagulation and levels of patient compliance. The newer anticoagulants are promoted as not needing to be monitored by coagulation testing, yet there are also no such tests available for these agents which may present problems in clinical settings.[427]

- There are well documented ways of dealing with bleeding events and reversing over anticoagulation associated with warfarin; no such antidotes are currently available for the newer agents.[418, 427]

- Caution is advised for the new agents in the case of impaired renal function, with recommendations including dose reduction or discontinuation.[418] Warfarin may be used in renally impaired patients and adjusted to anticoagulant effect.

If the level of INR control of patients taking warfarin could be improved through implementing strategies such as those discussed in preceding chapters, the benefits of the newer anticoagulants when compared to warfarin would become less and less significant.

The potential for improving the use of warfarin becomes particularly important when the discussion turns to the cost-effectiveness of these new, expensive agents. These agents are estimated by some sources to be around sixty-times more costly than warfarin.[427] Currently dabigatran is the only agent approved in Australia for stroke prevention in atrial fibrillation. Looking roughly at the basic costs involved in the medication itself and any monitoring requirements, dabigatran appears to be at

least five times more expensive than warfarin in the Australian setting (Table 36). Interestingly, the utilisation of PSM is unlikely to significantly alter the costs associated with warfarin but, as discussed in earlier sections, has the potential to improve INR control significantly, particularly for patients with poor control.

Table 36: Estimated annual costs of dabigatran compared to warfarin

	Medication costs (month)	Monitoring costs (month)	Monthly costs	Annual costs
Dabigatran (150mg bd)	$122.78	-	$122.78	$1473.36
Warfarin (5mg daily)	$15.12 (50 tabs) = $9.07 (30 tabs)	$13.80 per INR	$22.87	$275.97
Warfarin (5mg daily) +PSM	$9.07 (30 tabs)	$119.85 (24pk) $9.99 (2 strips)	$19.06	$228.72

Note: many assumptions have been made in the calculation of these costs:

- *The costs of visits to GPs have been excluded as most patients requiring anticoagulants are likely to require visits to their GP for conditions and prescriptions other than just the anticoagulant*
- *The dose of warfarin was taken to be 5mg daily as this is close to the average daily warfarin dose found by Kurnik et al.*[33]
- *Laboratory INR monitoring was costed at one test per month; PSM was costed at one test every two weeks and based on the cost of CoaguChek®XS test strips*
- *The cost of POC devices was excluded from the analysis (the current recommended retail price for a CoaguChek®XS POC device is $695)*
- *The cost of dabigatran and CoaguChek®XS test strips was taken from Symbion Pharmacy Services*[429] *and may differ between wholesalers and customers; the cost of warfarin was based on the maximum PBS price for either brand of 5mg tablets;*[430] *the cost of a laboratory INR test was based on the Medicare Schedule of Benefits.*[431]

Extrapolating these costs to the 200,000 people estimated to be taking warfarin in Australia currently, the annual cost of dabigatran would be approximately $295

million, while the cost of warfarin, with either form of monitoring, is closer to $50 million per year. This costing method obviously only takes into account the direct costs of each treatment without considering any potential benefits of the new agent compared to warfarin.

There are potential cost savings to be obtained through reductions in adverse events such as strokes and systemic embolism; however at Australian sites of the RE-LY trial these reductions were not found to be significant. This suggests that the benefits, and any potential for cost savings in Australian patients, are likely to be reduced, making dabigatran a more expensive option for stroke prevention in atrial fibrillation in this patient group. This is supported by a recent economic analysis which found that dabigatran (at 150mg twice daily) will be cost-effective only for patients at an increased risk of stroke or for whom INR control is likely to be poor.[432]

Economic analyses will provide varying results depending on which costs are included in the analysis and at this stage there are a number of unknowns affecting the reliability of cost-effectiveness analyses of new oral anticoagulant agents when compared to warfarin. The emerging agents obviously have higher direct costs of the medication itself when compared to warfarin and these can easily be costed. What is harder to cost is the potential utilisation of the newer agents. Warfarin is currently underused, particularly for stroke prevention in AF,[93] due to its narrow therapeutic margin and the associated inconvenience of monitoring, patient compliance, and physicians' fear of bleeding events.[98-100] The advantages of the newer anticoagulants may allay physicians' fears and perceptions of inconvenience, resulting in higher levels anticoagulant use than is currently seen and hence higher costs to healthcare payers. Such uncertainties are impacting on the willingness of governments around the world to approve and fund the new anticoagulant agents.

After an extensive evaluation process, the National Institute of Health and Clinical Excellence in the UK has recommended dabigatran as an option for stroke prevention in atrial fibrillation.[433] As such, it will now be funded through the National Health Service for this indication.[433] Similar evaluations were undertaken by the Pharmaceutical Management Agency of New Zealand, with the decision being made to approve and fund dabigatran for use in atrial fibrillation.[434]

In Australia, the Department of Health and Ageing has announced a review of anticoagulation therapies in atrial fibrillation to inform the Government on options for improving the health outcomes of patients treated with anticoagulants, including optimising the use of warfarin as well as the future role of newer agents.[435] The outcomes of this review will be watched with interest by consumers, health professionals and industry as the results will be important in shaping the future of anticoagulant use in this country.

One of the issues which prompted the review was additional concerns regarding patient safety which are emerging as the use of dabigatran for stroke prevention increases. As previously discussed, the incidence of AF, and the corresponding risk of stroke, increases with increasing age. The dabigatran product information suggests it is 85% renally excreted and the plasma concentration, and subsequently the anticoagulant effect, is increased by the coadministration of some other drugs, specifically amiodarone. This is particularly concerning as many of the patients who require anticoagulant therapy for AF are elderly patients, many of whom will have reduced renal function and may be taking amiodarone as part of their treatment regimen. Sub-group analyses of the RE-LY trial actually showed that in patients over the age of 75 years, the rates of major bleeding were increased for both dosing regimens of dabigatran when compared to warfarin.[436] Case reports are emerging raising further concern of the risks of major bleeding and the need for caution in the

elderly.[437] The ability to monitor the anticoagulant effects of warfarin may mean that it remains a safer choice for elderly patients with diminishing renal function, at least until there has been greater experience with the use of these newer agents.

For the time being, the new anticoagulant agents appear best suited as options for:

- Warfarin–treated patients who find it difficult to maintain a therapeutic INR;
- Those patients who are at an increased risk of drug-drug and drug-food interactions with warfarin; and
- Those patients for whom regular INR monitoring is difficult or impractical, particularly those who are not suitable for PSM.

The data that has emerged to date suggests that patients with an INR consistently in the therapeutic range, who are therefore at a low risk of stroke, may obtain little or no benefit from switching to a newer agent.

Warfarin remains an incredibly cheap medication that has the potential, through better management, to be even more effective in the prevention of thromboembolism than is currently reported. Despite a new generation of oral anticoagulants which do not require monitoring starting to emerge, their initial high cost, the uncertainty surrounding monitoring and reversal, and the potential for concern in the elderly, will mean they are unlikely to entirely replace warfarin in the short term. The potential for improving the management of warfarin to ensure its safe and effective use is likely to remain a priority for many years to come.

7.3 Recommendations and future directions

As the face of anticoagulation management changes with the introduction of new oral anticoagulant agents, warfarin remains an important and lifesaving medication for a range of patient groups and a range of conditions which have yet to undergo

clinical trials with the new alternatives. A number of steps can be taken within the Australian healthcare environment to improve the quality use of warfarin for patients for whom the new anticoagulants are yet to be verified as the solution to the anticoagulation challenge.

- Regardless of which data set is considered, literature suggests there is the potential for INR control among community-based and managed patients taking warfarin in Australia to be improved. The INR control of the Australian veteran population established in this research demonstrated room for improvement, with an average TTR barely above 60%. Newer agents may not be considered an acceptable alternative to warfarin for the veteran population, particularly as they are an ageing patient group (the median age of the study population was over 80 years). Strategies to improve anticoagulant control with warfarin, such as the implementation of PSM, should be investigated in this patient group.
- Veterans taking warfarin who live in outer regional areas may be less likely to achieve acceptable levels of INR control and further investigation of this finding, and its implications for the broader rural and regional populations of Australia, is warranted. People in outer regional areas may be a population likely to gain great benefit from the opportunity to undertake PSM.
- The web-based resource developed as part of this research should continue to evolve in response to changes in the anticoagulant environment. Content should be continually updated to reflect the changing agents available for anticoagulation. The online INR monitoring functionality would benefit from the input of further web-design expertise to enhance the user experience with what has otherwise been described as a valuable management platform.

- The tools and resources developed as part of this research to enable the implementation of pharmacist-delivered anticoagulation services could be used in the future to facilitate delivery of such services. However, pharmacists wishing to implement new and sustainable professional services should be encouraged to undertake a period of liaison with local stakeholders, particularly GPs and patients, to assess the potential sustainability of the service prior to implementation. It is likely that a dedicated practice facilitator funded through a professional organisation would be beneficial in assisting with liaison activities, professional service implementation and delivery.

- Professional organisations should strongly advocate for changes to the traditional model of Australian pharmacy practice to promote a remuneration model based on 'non-supply' services. Change in the remuneration structure of the healthcare system to enable pharmacist-delivered anticoagulation services to be directly remunerated through a Medicare-type arrangement is likely to be the key to ensuring the sustainability of such services.
- Implementation of PSM needs to be supported by health promotional activities to raise the awareness of the availability of point-of-care INR devices, of their place in therapy, and the usefulness of PSM as a warfarin management model. Awareness should be raised among all stakeholder groups, especially among consumers, GPs and pharmacists.

- Raised awareness should be supported by information and education to enable implementation of PSM. The web-based resource developed in this research may be an appropriate platform to raise awareness and provide access to educational materials.

- The self-monitoring training materials refined for use in this research have been reviewed by stakeholder organisations and piloted in the study population. It would now be appropriate for stakeholder organisations to formally endorse these materials for use in a national program facilitating PSM.

- A funding model should be developed to support the proposed PSM pathway. Recommendations include:

    - The training programs developed in this study should be funded and implemented on a national level. Funded training programs should cover the training program to credential pharmacists and the training program to train consumers.

    - An incentive scheme could be implemented to complement the rollout of accredited pharmacist training to ensure a critical mass of pharmacists is available to deliver the training service. This could be done in a manner similar to the incentive schemes that have been used in the Diabetes Medication Assistance Service and Pharmacy Asthma Management Service projects under the Fourth CPA.

    - It may be appropriate to look at government subsidies for portable INR monitoring devices and/or consumables to consumers, as is the case with the consumables for patients with diabetes who require blood glucose monitoring. It may be appropriate for conditions regarding training and ongoing QA to be attached to these subsidies.

- Training and credentialing of pharmacists to provide the PSM training service needs to be coordinated by a professional pharmacy organisation.

- Any national program to enable PSM should be accompanied by appropriate quality assurance measures, including initial and ongoing comparison pathology tests and an annual HMR. A partnership with the Royal College of Pathologists of Australasia may be appropriate to ensure ongoing QA is completed.

- Consideration should also be given to greater support for models of patient self-management, as are used in many international settings. The proposed pathway and patient training materials utilised in this study could be adopted, with minor modifications, to train patients for managing dose adjustments in addition to testing their INR.

- Alternatively, the materials for pharmacists could undergo minor modifications to facilitate pharmacists to be upskilled in providing dosage recommendations. Pharmacy indemnity insurers suggest this would be within a pharmacist's scope of practice, provided appropriate training had been undertaken. This could assist to remove some burden from doctors with the ever increasing workload in primary care. A pharmacist-delivered dosage adjustment model should be accompanied by a publically funded remuneration system.

- Self-monitoring is likely to be most beneficial for patients who exhibit poor INR control with routine care. These are the patient group who also appear to be most likely to benefit from the use of new anticoagulant agents. Further investigations to assess which intervention is likely to be most beneficial and cost-effective in this patient group could be valuable for informing prescribing decisions in practice.
- Self-monitoring was found to improve patient experiences of taking warfarin, independent of any change in INR control. The reassurance of

frequent evaluation of their anticoagulant control played a role in the improved experiences. It is likely that a cohort of patients will have a preference to continue taking warfarin with the reassurance of regular INR monitoring when faced with the choice of transferring to a new anticoagulant agent for which no monitoring is available.

- The new oral anticoagulant agents are certain to have a role to play in improving outcomes for patients requiring anticoagulation therapy. It remains to be seen to what extent they will be used and for what conditions they will prove to be more beneficial than well-controlled warfarin therapy. Head to head comparison trials or extensive clinical experience are likely to be needed to establish which of the new agents is likely to play the greatest role in safely and effectively replacing warfarin in the future.

7.4 Conclusion

The results of these projects suggest that expansion of the professional services offered by pharmacists has the potential to improve the quality and control of warfarin therapy in Australia. Changes in remuneration for healthcare services are likely to increase the viability of pharmacist-delivered INR services and the uptake of PSM. Despite the arrival of newer oral anticoagulant agents, the use of warfarin is likely to continue for many years. Optimising warfarin management is arguably the safest and most clinically and cost-effective option for preventing and treating thromboembolism. Pharmacists can play an important role in improving warfarin management by embracing opportunities to deliver professional services aimed at optimising outcomes for Australians taking warfarin.

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